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(54) Imidazole derivatives, processes for the preparation of the same, pharmaceutical compositions comprising the same, the use of the same for the manufacture of medicaments of therapeutic value, and intermediates formed during said processes.

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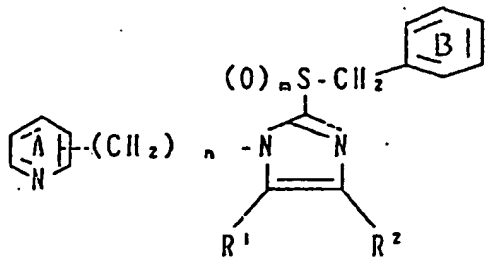
Description

This invention relates to a novel imidazole derivative and processes for preparing same. More particularly, it relates to an imidazole derivative of the formula:



(I)

wherein Ring A is a 2- or 4-pyridyl group or a 2- or 4-pyridyl group having a substituent selected from a C_{1-4} alkyl group and a C_{1-4} alkoxy group; Ring B is a phenyl group having one substituent selected from an amino group, a mono(C_{1-4} alkyl)amino group, a di(C_{1-4} alkyl)amino group, and a morpholino group; R^1 and R^2 are hydrogen atoms or are combined together to form a group of the formula: $-(CH_2)_q-$; m is 1; n is 0 or 1; and q is 3 or 4, or a pharmaceutically acceptable acid addition salt thereof.

Excessive gastric acid secretion is one of causative factors of peptic ulcer diseases such as gastric ulcer and duodenal ulcer. Since the acid secretion by gastric parietal cells is known to be induced by histamine, acetylcholine or gastrin, cholinergic receptor blockers (e.g., atropine) and histamine H_2-receptor blockers (e.g., cimetidine) which antagonize these stimuli in living tissues have been used for treatment of such ulcer diseases [Medicina, 23(4) 560-565 (1986)].

Moreover, benzimidazole compounds such as omeprazole have been recently found to show the antisecretory effects due to their inhibitory effect on the enzymatic activity of H^+/K^+ ATPase (i.e., the enzyme which plays an important role in concentration and/or secretion of gastric acid) (Japanese Patent Publication (unexamined) No. 141783/1979).

However, among these known drugs, cholinergic receptor blockers are still unsatisfactory for clinical use because of strong toxicity (e.g., atropine toxicosis). Cimetidine, one of the histamine H_2 receptor blockers, is also known to have unfavorable side effects such as anti-androgen effect and prolactin release-stimulating effect.

EP-A-0125756 and EP-A-0174717 describe various substituted sulfinyl-benzimidazole derivatives which are useful as anti-ulcer agents. In particular, these references respectively disclose the use of 2-(2-pyridylmethyl)-1-phenyl-1H-benzimidazole and 2-(2-dimethylaminobenzylsulfinyl)-1H-benzimidazole for treating ulcers.

As a result of various investigations, we have now found that the compound (I) of the present invention and a salt thereof show potent inhibitory effect against gastric acid secretion and is useful for therapeutic treatment or prophylaxis of peptic ulcer diseases. For example, when the effect of a test compound on gastrin-induced gastric acid secretion was examined by oral administration to rats, each one of 1-(2-pyridyl)-2-[2-(1-pyrrolyl)benzylsulfinyl]imidazole, 1-(3-methyl-2-pyridyl)-2-[2-(dimethylamino)benzylsulfinyl]-imidazole and 1,4,5,6-tetrahydro-1-(2-pyridyl)-2-[2-(diethylamino)-benzylsulfinyl]cyclopenta[d]imidazole at the dose of 30 mg/kg showed more than 70 % decrease in gastric acid secretion as compared with non-administered group of rats. On the other hand, when the effect of a test compound on the enzyme activity of H^+/K^+ ATPase prepared from the porcine gastric mucosa was examined, IC_{50} (i.e., the concentration required to induce 50% inhibition of said enzymatic activity) of 1,4,5,6-tetrahydro-1-(2-pyridyl)-2-[2-(diethylamino)benzylsulfinyl]cyclopenta[d]imidazole was about 10 μM and IC_{50} of 1-(2-pyridyl)-2-[2-(cyclohexylamino)benzylsulfinyl]imidazole and 1-(4-methoxy-6-methyl-2-pyridyl)-2-[2-(diethylamino)-benzylsulfinyl]imidazole were less than 10 μM.

Examples of the compound of the present invention are those of the formula (I) in which Ring A is a 2- or 4-pyridyl group which may optionally have a substituent selected from a lower alkyl group such as methyl group or ethyl group or a lower alkoxy group such as methoxy group, ethoxy group or isopropoxy group. Ring B is a phenyl group having one substituent selected from amino group, a mono- or di(lower alkyl)amino group such as methylamino group, ethylamino group, dimethylamino group, diethylamino group or dipropylamino group, or a morpholino group. pyrrolidinyl group or piperidino group; R^1 and R^2 are

hydrogen atom or are combined together to form trimethylene group or tetramethylene group; m is 1; and n is 0 or 1.

Among them, preferred examples of the compound of the invention are those of the formula (I) in which Ring A is 2- or 4- pyridyl group which may optionally have one or two substituent(s) selected from a C_{1-4} alkyl group and a C_{1-4} alkoxy group; Ring B is phenyl group one substituent selected from a di(C_{1-4} alkyl)amino group and a morpholino group; R^1 and R^2 are hydrogen atom or are combined together to form trimethylene group; m is 1; and n is 0 or 1.

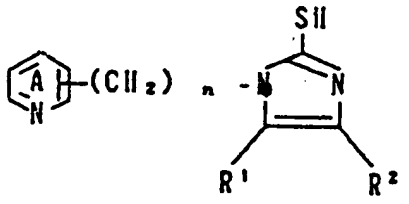
More preferred examples of the compound of the invention are those of the formula (I) in which Ring A is 2- or 4-pyridyl group, a 3-, 4- or 5-(C_{1-4} alkoxy)-2-pyridyl group or a 3-, 4-, 5- or 6-(C_{1-4} alkyl)-2-pyridyl group; Ring B is a 2-morpholinophenyl group or a 2-di(C_{1-4} alkyl)aminophenyl group; R^1 and R^2 are hydrogen atom or are combined together to form trimethylene group; m is 1; and n is 0 or 1.

Most preferred examples of the compound of the invention are those of the formula (I) in which Ring A is 2-pyridyl group or a 3-(C_{1-4} alkyl)-2-pyridyl group; Ring B is a 2-(C_{1-4} alkyl)aminophenyl group; R^1 and R^2 are hydrogen atom or are combined together to form trimethylene group; m is 1; and n is 0.

While the compound (I) of the present invention in which m is 1 may exist in the form of two optically active isomers due to an asymmetric sulfoxide group, the present invention includes within its scope either one of these isomers and a mixture thereof.

According to the present invention, the compound (I) or a salt thereof can be prepared by the steps of:

i) condensing a mercaptoimidazole compound of the formula:



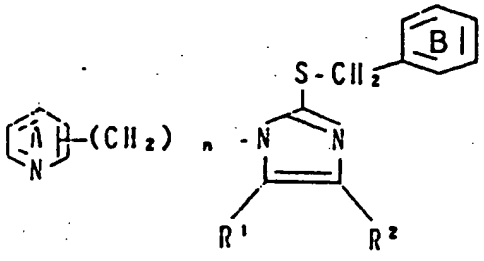
(III)

wherein Ring A, R^1 R^2 and n are the same as defined above, or a salt thereof with a toluene compound of the formula:

(IV)

wherein X is a reactive residue and Ring B is the same as defined above, or a salt thereof,

ii) oxidizing the resultant product of the formula:



(II)

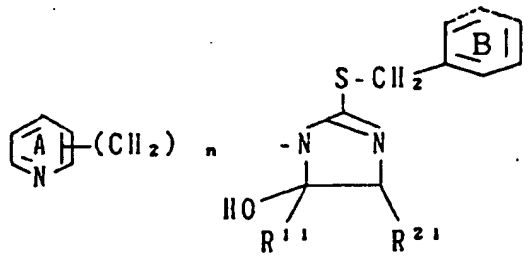
wherein Ring A, Ring B, R^1, R^2 and n are the same as defined above, and

iii) if required, further converting the product into a salt thereof.

Alternatively, the compound (I) in which R^1 and R^2 are combined together to form a group of the formula: $-(CH_2)_q-$ (wherein q is the same as defined above) or a salt thereof can be prepared by the steps

of:

iv) dehydrating a compound of the formula:



(V)

wherein R^{11} and R^{21} are combined together to form a group of the formula: $-(CH_2)_q-$ and Ring A, Ring B, q and n are the same as defined above,

v) oxidizing the resultant product, and

vi) if required, further converting the product into a salt thereof.

The condensation of the mercaptoimidazole compound (III) and the toluene compound (IV) can be conducted in the presence or absence of an acid acceptor in an inert solvent. Any groups which enable to form C-S bond through reaction with a mercapto group can be used as the reactive residue "X" of the toluene compound (IV). Such reactive residue X includes, for example, a halogen atom, an alkylsulfonyloxy group (e.g., methylsulfonyloxy group), an arylsulfonyloxy group (e.g., toluenesulfonyloxy group, benzenesulfonyloxy group) and the like. The compound (IV) which has amino group, a N-substituted amino group and the like on the benzene ring may, if required, be used for the reaction in the form of an organic or inorganic acid addition salt such as hydrochloride, hydrobromide, sulfate, nitrate, formate, oxalate or methanesulfonate. On the other hand, the compound (III) may, if required, be used for the reaction in the form of an organic or inorganic acid addition salt (e.g., hydrochloride, hydrobromide, sulfate, nitrate, formate, oxalate or methanesulfonate), an alkali metal salt (e.g., sodium salt or potassium salt), an alkaline earth metal salt (e.g., calcium salt or magnesium salt), and a quaternary ammonium salt (e.g., tetramethylammonium salt). A lower alkanol, dimethylformamide, dimethylsulfoxide, water and the mixture thereof are suitable as the solvent. Suitable examples of the acid acceptor include inorganic bases such as an alkali metal hydroxide, an alkali earth metal hydroxide, an alkali metal carbonate, an alkali metal bicarbonate, an alkali metal alkoxide, an alkali metal amide, an alkali metal fluoride, an alkali metal hydride, or organic bases such as pyridine, a tri-lower alkylamine, a lower alkyl lithium, a quaternary ammonium hydroxide (e.g., tetra n-butyl ammonium hydroxide), and the like. It is preferred to carry out the reaction at -20 °C to 170 °C, especially -10 to 100 °C.

On the other hand, the dehydration of the imidazole derivative (V) can be conducted in the presence of a dehydrating agent in an inert solvent. Suitable examples of the dehydrating agent include organic acids such as formic acid, trifluoroacetic acid, p-toluenesulfonic acid, benzenesulfonic acid or camphorsulfonic acid, mineral acids such as hydrochloric acid or sulfonic acid or a mixture of a halogenating agent (e.g., phosphrus tribromide, phosphorus trichloride or phosphorus oxychloride) and a base (e.g., pyridine or triethylamine) and the like. The compound (V) may, if required, be used for the reaction in the form of an organic or inorganic acid addition salt such as hydrochloride, hydrobromide, sulfate, nitrate, formate, oxalate or methanesulfonate. It is preferred to carry out the reaction at -20 °C to 150 °C, especially -10 °C to 100 °C.

The oxidation of the above-obtained compound (II) [including the dehydration product of the imidazole derivative (V)] is conducted by treating it with an oxidative agent.

Conventional oxidative agents such as peroxy acids (e.g., m-chloroperbenzoic acid, perbenzoic acid or peracetic acid), an alkali metal hypochlorite, an alkali metal chlorite, an alkali metal periodate, tetra n-butyl ammonium periodate, tert.- butyl hydroperoxide, iodoxybenzene, and the like can be used for the reaction. A lower alkanol, methylene chloride, chloroform, tetrahydrofuran, dioxane, water and the mixture thereof are suitable as the solvent. It is preferred to carry out the reaction at -70 °C to 100 °C, especially -50 °C to 20 °C. In this reaction, a sulfinyl-imidazole compound (I) (m = 1) is obtained by using an equimolar amount or a little excess amount of the oxidative agent, and a sulfonyl-imidazole compound (I) (m = 2) is obtained by using not less than two equimolar amount of the oxidative agent.

The intermediate (II) obtained by the above-mentioned reaction is a novel compound, and the substituent(s) on the Ring A and/or B thereof may be, if required, modified or converted to other substituent-

(s) before the oxidation step. For example, the compound (II) having amino group on the Ring A and/or B may be obtained by conventional reduction of the compound (II) having nitro group thereon, or by hydrolysis of the corresponding N-phthalimido or N-tri lower alkylphenylsulfonylamido compound (II). Alternatively, the compound (II) having one or two substituent(s) selected from a lower alkanoylamino group, a lower alkylsulfonylamino group, formylamino group, a lower alkylamino group, an arylcarbonylamino group, a lower alkoxycarbonylamino group and a substituted phenylsulfonylamino group on the Ring A and/or B thereof may be obtained by conventional acylation or alkylation of the compound (II) having amino group, an N-alkylamino group or an N-acylamino group on said Ring A and/or B.

Because of the potent inhibitory effect against gastric acid secretion and/or potent inhibitory effect on the enzymatic activity of H^+/K^+ ATPase, the imidazole compound (I) of the present invention and a salt thereof are useful for therapeutic treatment and/or prophylaxis of peptic ulcer diseases such as gastric ulcer and duodenal ulcer. The imidazole compound (I) and a salt thereof can be used without unfavorable side effects such an anti-androgen or prolactin release-stimulating effects as observed in histamine H_2-receptor blockers. Moreover, since the imidazole compound (I) and a salt thereof may include a group of compounds which inhibit effectively the gastric acid secretion without affecting the enzyme activity of H^+/K^+ ATPase, such compounds may be used as anti-ulcer agents which are different in mechanism of action from the known H^+/K^+ ATPase inhibitors such as omeprazole.

The compound (I) can be used for pharmaceutical use either in the free form or in the form of a salt thereof. Suitable salts of the compound (I) for pharmaceutical use include, for example, pharmaceutically acceptable salts such as inorganic acid addition salts (e.g., hydrochloride, hydrobromide, hydroiodide, sulfate, nitrate), organic acid addition salts (e.g., formate, oxalate, methanesulfonate, glucuronate), and the like. Such salts may be obtained by treating the free base of the compound (I) with a stoichiometrically equimolar amount of the acid.

The dose of the compound (I) or a salt thereof may vary depending on the age, condition and body weight of patients, the kind and severity of diseases to be treated and administration route, etc, but may usually be about 0.05 to about 50 mg/kg, preferably about 0.1 to about 20 mg/kg, per day.

The compound (I) and a salt thereof may be administered either orally or parenterally. When administrated orally, the pharmaceutical preparation may be in the solid form such as tablets, powders, capsules or suppositories. These preparations may contain pharmaceutical excipient, binder, diluent, disintegrator or lubricant. The pharmaceutical preparation for oral administration may also be in liquid form such as aqueous or oily suspension, solution, sirup or elixir. Moreover, when administered parenterally, the pharmaceutical preparation may be used in the form of injections.

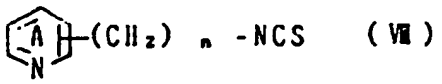
Concomitantly, the starting compound (III) in which R^1 and R^2 are hydrogen atom may be prepared by the steps of reacting a pyridine compound of the formula:

(VI)

wherein Ring A and n are the same as defined above, with a iso (thio) cyanate compound of the formula:

$$Z=C=NCH_2CH(OR^3)_2 \quad \text{(VII)}$$

wherein R^3 is an alkyl group and Z is oxygen atom or sulfur atom, in an inert solvent, treating the thus-obtained (thio) urea compound with an organic or inorganic acid to give the corresponding cyclic compound, and when Z is oxgen atom, further treating the cyclic compound with a sulfur agent such as Lawesson's Reagent [2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane-2,4-disulfide], 2,4-diethoxy-1,3-dithia-2,4-diphosphetane-2,4-disulfide or phosphorus petasulfide. Alternatively, the starting compound (III) in which R^1 and R^2 are combined together to form a group of the formula: - $(CH_2)_q$-, (wherein q is the same as defined above) may be prepared by condensing 2-aminocyclohexanone or 2-aminocyclopentanone with a compound of the formula:



(VII)

wherein Ring A and n are the same as defined above, in the presence of triethylamine, and dehydrating the product in the same manner as described in the dehydration reaction of the imidazole derivative (V). The starting compound (V) may be prepared by condensing 2-aminocyclohexanone or 2-aminocyclopentanone with the compound (VIII) in the presence of triethylamine, and then condensing the product with the toluene compound (IV).

Practical and presently preferred embodiments of the present invention are illustratively shown in the following Examples.

Example 1

(1) 3.0 g of 1-(2-pyridyl)-2-mercaptoimidazole are dissolved in 50 ml of ethanol, and 16.9 ml of a 2N-aqueous sodium hydroxide solution are added thereto under ice-cooling. 3.84 g of m-dimethylaminobenzyl chloride hydrochloride are added to the mixture and stirred at room temperature for 2 hours. After the solvent is distilled off, water is added to the residue, and the mixture is extracted with ethyl acetate. The extract is washed with water, dried and evaporated to remove the solvent. The residue is recrystallized from a mixture of ethyl acetate and n-hexane, whereby 3.95 g of 1-(2-pyridyl)-2-(3-dimethylaminobenzylthio)imidazole are obtained.

Yield 75%

M.p. 79-80 °C

(2) A solution of 3.73 g of the product obtained above in 100 ml of methylene chloride is cooled to -40 °C under argon gas atmosphere. 5.32 g of 80% m-chloroperbenzoic acid are added thereto gradually. The mixture is stirred at the same temperature for 1 hour. The reaction mixture is washed with a saturated aqueous sodium bicarbonate solution, dried and evaporated to remove the solvent. The residue is recrystallized from methanol, whereby 1.48 g of 1-(2-pyridyl)-2-(3-dimethylaminobenzylsulfinyl)-imidazole are obtained.

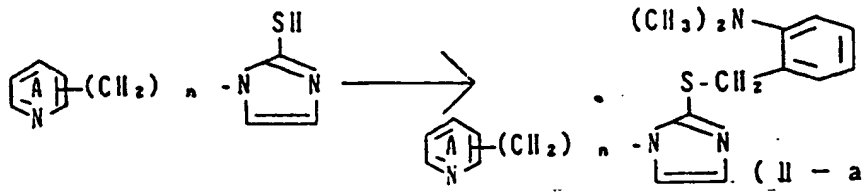
Yield 55%

M.p. 177-179 °C

Examples 3 to 25

(1) The corresponding starting compounds are treated in the same manner as described in Example 1-(1) to give the compounds shown in Table 1.

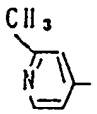
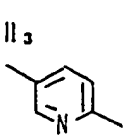
Table 1

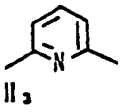


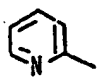
(II - a)

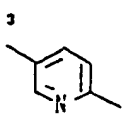
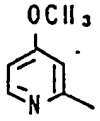
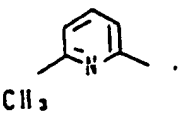
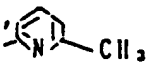
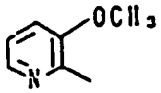
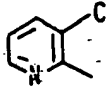
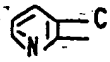
(wherein n= 1 in Example 14, and n=0 in Example 1 to 8, 12 and 15 to 25)

Ex. Nos.	Compound(II-a) Ring A	Properties*)

7-(1)		oil
8-(1)		M.p. 51 to 53.5°C (recrystallized from ethyl acetate and n-hexane)

12-(1)		oil; NMR δ :2.96(s,6H,$N(CH_3)_2$),3.96 (s,3H,OCH_3),4.61(s,2H,SCH_2) Mass(m/e):340(M^+), 134

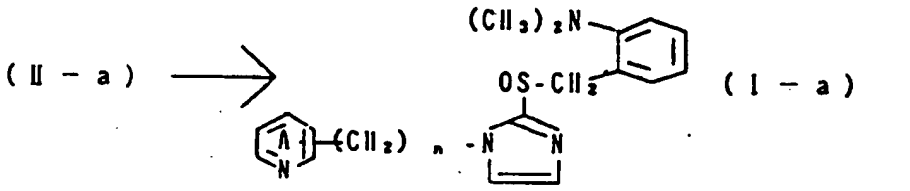
14-(1)		oil; NMR, δ :2.66(s,6H,$N(CH_3)_2$), 4.38(s,2H,SCH_2),5.08(s,2H,NCH_2) Mass(m/e):324(M^+)
15-(1)		oil; NMR, δ :2.68(s,6H,$N(CH_3)_2$), 4.58(s,2H,SCH_2) Mass(m/e):310(M^+)

17-(1)		oil; NMR, δ :2.32(s,3H, ), 2.67(s,6H,$N(CH_3)_2$), 4.57(s,2H,SCH_2) Mass(m/e):324(M^+)
18-(1)		oil; NMR, δ :2.60(s,6H,$N(CH_3)_2$), 4.45(s,2H,SCH_2) Mass(m/e):310(M^+)
22-(1)		oil; NMR, δ :2.68(s,6H,$N(CH_3)_2$), 3.85(s,3H,OCH_3),4.58(s,2H,SCH_2) Mass(m/e):340(M^+)
23-(1)		oil; NMR, δ :2.54(s,3H, ), 2.68(s,6H,$N(CH_3)_2$), 4.58(s,2H,SCH_2) Mass(m/e):324(M^+)
24-(1)		oil; NMR, : δ 2.63(s,6H,$N(CH_3)_2$), 3.81(s,3H,OCH_3),4.48(s,2H,SCH_2) Mass(m/e):340(M^+)
25-(1)		oil; NMR, δ :2.08(s,3H, ), 2.61(s,6H,$N(CH_3)_2$), 4.45(s,2H,SCH_2) Mass(m/e):324(M^+)

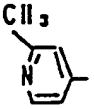
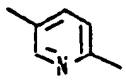
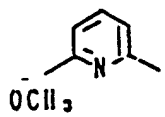
*) note: NMR is measured in $CDCl_3$

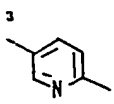
(2) The products obtained above are treated in the same manner as described in Example 1-(2) to give the compounds shown in Table 2.

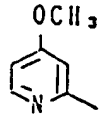
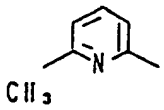
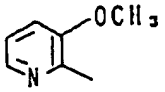
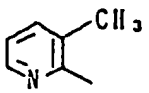
Table 2



(wherein n=1 in Example 14, and n=0 in Examples 1 to 8, 12, and 15 to 25)

Ex. Nos.	Compound(I-a) Ring A	Properties*)
7-(2)		M.p. 117 to 119 °C(recrystallized from chloroform and isopropyl ether)
8-(2)		M.p. 81.5 to 83.5 °C(recrystallized from ethyl acetate and n-hexane)
12-(2)		M.p. 102 to 104 °C(recrystallized from ethyl acetate and n-hexane)

14-(2)		M.p. 93 to 94 °C(recrystallized from ethyl acetate and ether)
15-(2)		M.p. 104 to 105 °C(recrystallized from ethyl acetate and n-hexane)
17-(2)		oil; NMR, δ :2.38(s,3H,CH_3), 2.63(s,6H,$N(CH_3)_2$), 4.85(ABq,2H,J=12.5Hz,SCH_2)
18-(2)		M.p. 102 to 104 °C(recrystallized from chloroform and isopropyl ether)

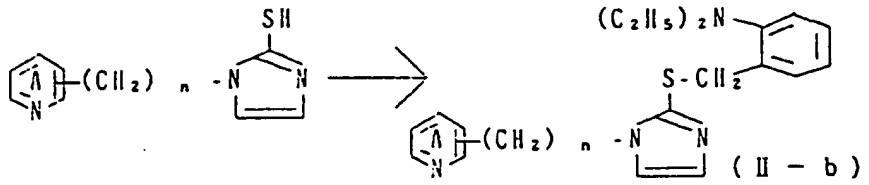
22-(2)		M.p. 117 to 120 °C(recrystallized from isopropyl alcohol and isopropyl ether)
23-(2)		Oxalate ** M.p. 82 to 84 °C(decomp.)
24-(2)		oil; NMR, δ :2.61(s,6H,N(CH_3)$_2$),3.83 (s,3H,OCH_3),4.80(ABq,2H,J=12.5Hz,SCH_2) Mass(m/e):356(M^+),134
25-(2)		M.p. 89 to 91 °C (recrystallized from ethyl acetate and n-hexane) NMR, δ :2.11(s,3H, ), 2.59(s,6H,N(CH_3)$_2$), 4.80(ABq,2H,J=12.5Hz, SCH_2)

*) note: NMR is measured in $CDCl_3$

Examples 26 to 31

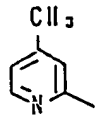
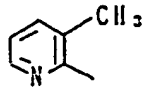
(1) The corresponding starting compounds are treated in the same manner as described in Example 1-(1) to give the compounds shown in Table 3.

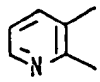
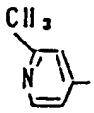
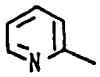
Table 3



(II - b)

(wherein n=0)

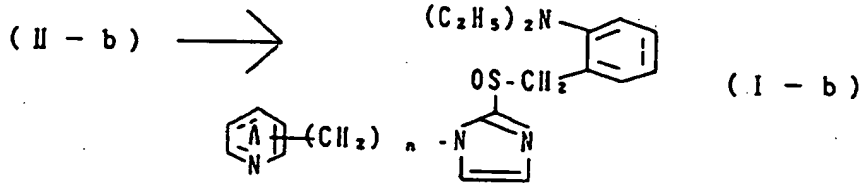
Ex. Nos.	Compound(II-b) Ring A	Properties*)
26-(1)		oil; NMR, δ :0.95(t,6H,$NCH_2\underline{CH_3}$), 2.37(s,3H,C-CH_3),2.95(q,4H,$N\underline{CH_2}CH_3$), 4.56(s,2H, SCH_2) Mass(m/e):352(M^+),146
27-(1)		oil; NMR, δ :0.87(t,6H,$NCH_2\underline{CH_3}$), 2.04(s,3H,C-CH_3),2.88(q,4H,$N\underline{CH_2}CH_3$), 4.44(s,2H, SCH_2) Mass(m/e):352(M^+),146

29-(1)		oil; NMR, δ :0.88(t,6H,$NCH_2\underline{CH_3}$), 2.89(q,4H,$N\underline{CH_2}CH_3$),3.79(s,3H,OCH_3), 4.47(s,2H, SCH_2) Mass(m/e):368(M^+),146
30-(1)		oil
31-(1)		oil; NMR, δ :0.94(t,6H,$NCH_2\underline{CH_3}$), 2.95(q,4H,$N\underline{CH_2}CH_3$), 4.95(s,2H, SCH_2) Mass(m/e):329(M^++1),146

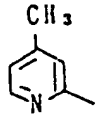
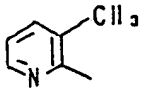
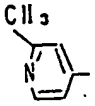
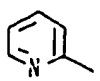
*) note: NMR is measured in $CDCl_3$

(2) The products obtained above are treated in the same manner as described in Example 1-(2) to give the compounds shown in Table 4.

Table 4



(wherein n=0)

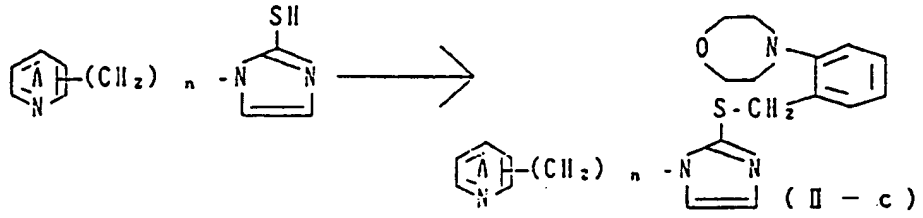
Ex. Nos.	Compound(I-b) Ring A	Properties*)
26-(2)		M.p. 110 to 112 °C(recrystallized from ether)
27-(2)		M.p. 81 to 83 °C(recrystallized from ether and n-hexane)
29-(2)		oil; NMR, δ :0.87(t,6H,$NCH_2\underline{CH_3}$), 3.81(s,3H,OCH_3), 4.80(ABq,2H, SCH_2) Mass(m/e):384(M^+),162
30-(2)		M.p. 121 to 123 °C(recrystallized from isopropyl ether)
31-(2)		M.p. 115 to 116 °C(recrystallized from methylene chloride and n-hexane)

*) note: NMR is measured in $CDCl_3$

Examples 35 to 50

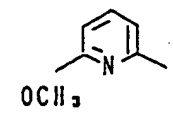
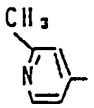
(1) The corresponding starting compounds are treated in the same manner as described in Example 1-(1) to give the compounds shown in Table 5.

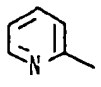
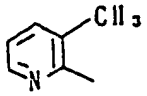
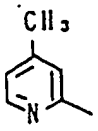
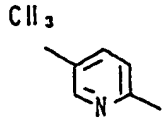
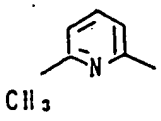
Table 5

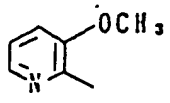
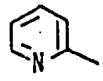


(II - c)

(wherein n=1 in Example 41, and n=0 in Examples 35 to 40 and 42 to 50)

Ex. Nos.	Compound(II-c) Ring A	Properties*)
35-(1)		M.p. 119 to 121.5°C (recrystallized from ethyl acetate and n-hexane)
40-(1)		oil

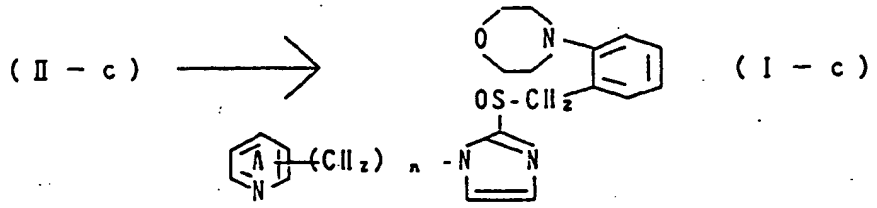
41-(1)		oil; NMR, δ :4.39(s,2H,SCH_2), 5.04(s,2H,NCH_2N) Mass(m/e):367(M^++1),175
42-(1)		M.p. 137 to 138°C (recrystallized from ethyl acetate and n-hexane)
43-(1)		oil; NMR, δ :2.06(s,3H,CH_3), 4.44(s,2H,SCH_2) Mass(m/e):366(M^+),175
44-(1)		M.p. 109 to 111°C (recrystallized from ethyl acetate and n-hexane)
45-(1)		M.p. 98 to 100°C (recrystallized from ethyl acetate and isopropyl ether)
46-(1)		M.p. 114 to 116°C (recrystallized from ethyl acetate and n-hexane)

48-(1)		M.p. 124 to 126°C (recrystallized from ethyl acetate and n-hexane)
50-(1)		M.p. 112 to 113°C (recrystallized from ethyl acetate, ether and n-hexane)

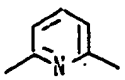
*) note: NMR is measured in $CDCl_3$

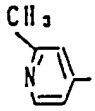
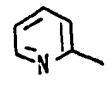
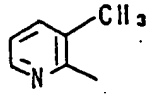
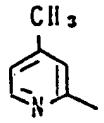
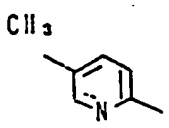
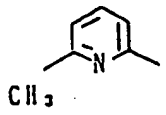
(2) The products obtained above are treated in the same manner as described in Example 1-(2) to give the compounds shown in Table 6.

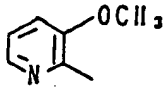
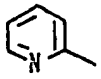
Table 6



(wherein n=1 in Example 41, and n=0 in Examples 35 to 40 and 42 to 50)

Ex. Nos.	Compound(I-c) Ring A	Properties*)
35-(2)		M.p. 139 to 141°C (recrystallized from ethyl acetate and n-hexane)

40-(2)		M.p. 91 to 96°C (recrystallized from isopropyl ether)
41-(2)		oil; NMR, δ :4.81(ABq,2H,SCH_2), 5.35(ABq,2H,NCH_2N) Mass(m/e):383(M^++1),176
42-(2)		M.p. 150 to 152°C (recrystallized from ethyl acetate)
43-(2)		M.p. 129 to 130°C (recrystallized from ethyl acetate and n-hexane)
44-(2)		M.p. 155.5 to 157.5°C (recrystallized from chloroform and n-hexane)
45-(2)		M.p. 135 to 137°C (recrystallized from ethyl acetate)
46-(2)		M.p. 124 to 126°C (recrystallized from ethyl acetate and n-hexane)

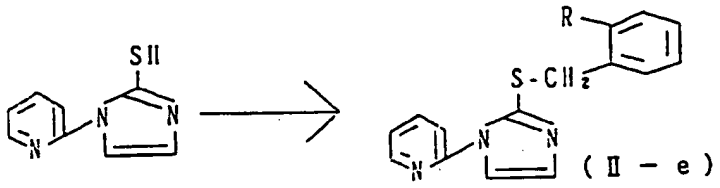
48-(2)		M.p. 130 to 132°C (recrystallized from ethyl acetate and n-hexane)
50-(2)		M.p. 112 to 115°C (recrystallized from ethyl acetate)

*) note: NMR is measured in $CDCl_3$

Example 59

(1) The corresponding starting compound is treated in the same manner as described in Example 1-(1) to give the compound shown in Table 9.

Table 9



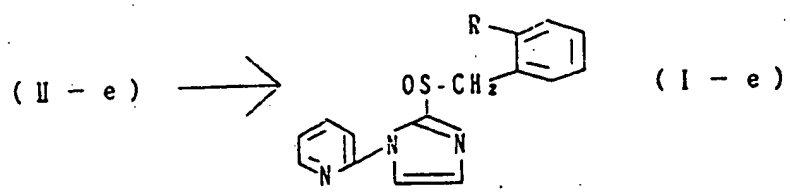
(II - e)

Ex. Nos.	Compound(II-e) R	Properties*)
59-(1)	$-N(n-C_3H_7)_2$	oil; NMR, δ :0.79(t,6H,J=7Hz,CCH_3), 4.61(s,2H, SCH_2) Mass(m/e):367(M^++1),190

*) note: NMR is measured in $CDCl_3$

(2) The product obtained above is treated in the same manner as described in Example 1-(2) to give the compound shown in Table 10.

Table 10



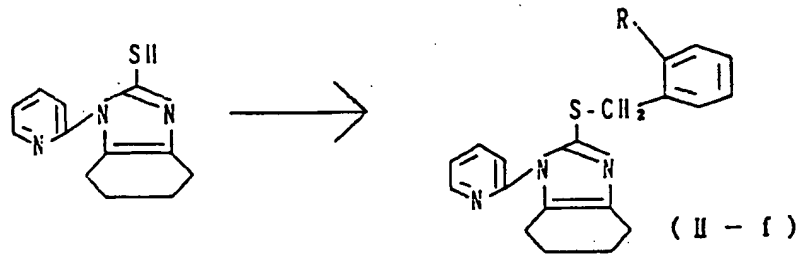
Ex. Nos.	Compound(I-e) R	Properties*)
59-(2)	$-N(n-C_3H_7)_2$	oil; NMR, δ :0.76(t,6H,J=7Hz, $CH_2CH_2CH_3$),4.88(ABq,2H,SCH_2) liquid IRν_{max} (cm^{-1}): 1050 (S-O)

*) note: NMR is measured in $CDCl_3$

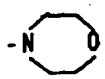
Examples 65 to 66

(1) The corresponding starting compounds are treated in the same manner as described in Example 1-(1) to give the compounds shown in Table 11.

Table 11



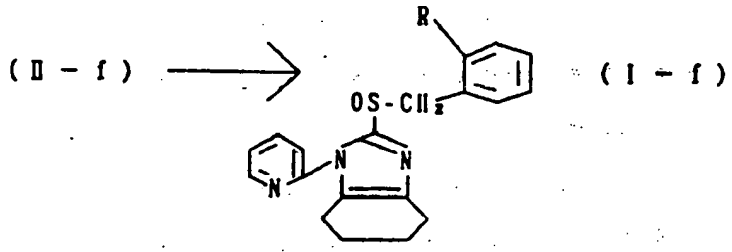
(II - f)

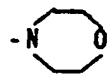
Ex. Nos.	Compound(II-f) R	Properties*)
65-(1)	$-N(CH_3)_2$	oil; NMR, δ :1.70-1.97(m,4H,CH_2),2.40 -2.87(m,4H,=CCH_2), 2.60(s,6H,$N(CH_3)_2$),4.39(s,2H, SCH_2) Mass(m/e):364(M^+),134
66-(1)		oil; NMR, δ :1.76-1.89(m,4H,CH_2),2.43 -2.71(m,4H,=CCH_2), 2.73-2.87(m,4H,NCH_2),3.68 -3.81(m,4H,OCH_2),4.40(s,2H, SCH_2) Mass(m/e):406(M^+)

*) note: NMR is measured in $CDCl_3$

(2) The products obtained above are treated in the same manner as described in Example 1-(2) to give the compounds shown in Table 10.

Table 12



Ex. Nos.	Compound(I-f) R	Properties*)
65-(2)	$-N(CH_3)_2$	oil; NMR, δ :2.59(s,6H,$N(CH_3)_2$), 4.80(ABq,2H, SCH_2) FABMass(m/e):381(M^++1)
66-(2)		oil; NMR,δ :4.82(ABq,2H, SCH_2) FABMass(m/e):423(M^++1)

*) note: NMR is measured in $CDCl_3$

Example 67

(1) A solution of 7.53 g of 2-(2-dimethylaminobenzylthio)-1,3a,4,5,6,6a-hexahydro-6a-hydroxy-1-(2-pyridyl)cyclopenta[d]imidazole and a catalytic amount of p-toluenesulfonic acid in 100 ml of toluene is refluxed for 1 hour. The reaction mixture is evaporated to remove the solvent, water is added to the residue, and the aqueous mixture is neutralized with an aqueous sodium bicarbonate solution. The mixture is extracted with chloroform. The extract is dried and evaporated to remove the solvent, whereby 3.94 g of 1,4,5,6-tetrahydro-2-(2-dimethylaminobenzylthio)-1-(2-pyridyl)cyclopenta[d]imidazole are obtained.

Yield 55%

M.p. 115 to 117 °C (recrystallized from ethyl acetate and n-hexane)

(2) The product obtained above is treated in the same manner as described in Example 1-(2) to give 1,4,5,6-tetrahydro-2-(2-dimethylaminobenzylsulfinyl)-1-(2-pyridyl)cyclopenta[d]imidazole.

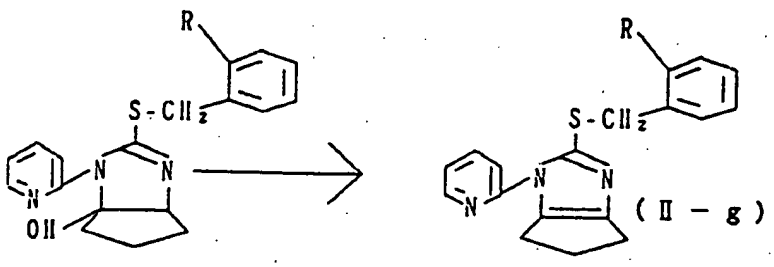
Yield 74%.

M.p. 139.5 to 141 °C (recrystallized from ethyl acetate and n-hexane)

Examples 68 to 70

(1) The corresponding starting compounds are treated in the same manner as described in Example 67-(1) to give the compounds shown in Table 13.

Table 13

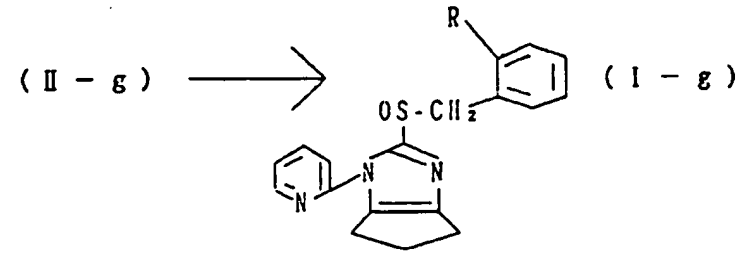


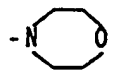
(II - g)

Ex. Nos.	Compound(II-g) R	Properties
68-(1)	$-N(C_2H_5)_2$	M.p. 106 to 108°C (recrystallized from ethyl acetate and n-hexane)
70-(1)		M.p. 115 to 116°C (recrystallized from isopropyl ether)

(2) The products obtained above are treated in the same manner as described in Example 1-(2) to give the compounds shown in Table 14.

Table 14



Ex. Nos.	Compound(I-g) R	Properties
68-(2)	$-N(C_2H_5)_2$	M.p. 107 to 109 °C (recrystallized from ethyl acetate and n-hexane)
70-(2)		M.p. 135 to 136.5 °C (recrystallized from ethyl acetate)

Example 71

(1) 1-(2-pyridyl)-2-mercaptoimidazole and (2,4,6-trimethylphenyl)sulfonylaminobenzyl chloride are treated in the same manner as described in Example 1-(1) to give 1-(2-pyridyl)-2-[2-(2,4,6-trimethylphenyl)-sulfonylaminobenzylthio]imidazole.

Yield 87%

M.p. 154 to 156 °C (recrystallized from isopropyl alcohol)

(2) A mixture of 2 g of the product obtained above, 2.5 ml of anisole and 15 ml of methanesulfonic acid is stirred at room temperature for 20 hours. After the reaction, the mixture is added to water and extracted with ethyl acetate. The extract is washed with a saturated aqueous sodium chloride solution, dried and evaporated to remove the solvent, whereby 1.1 g of 1-(2-pyridyl)-2-(2-aminobenzylthio)-imidazole are obtained as an oil

Yield 93%

Mass (m/e):282(M^+), 106

^{1}H-MNR ($CDCl_3$,δ):3.9(br,2H,NH_2),4.43(s,2H,SCH_2)

(3) The product obtained above is treated in the same manner as described in Example 1-(2) to give 1-(2-pyridyl)-2-(2-aminobenzylsulfinyl)imidazole.

M.p. 145 to 146 °C (recrystallized from isopropyl alcohol)

Example 73

(1) 100 mg of 60% sodium hydride are suspended in 2 ml of dimethyl formamide, and a solution of one g of 1-(2-pyridyl)-2-[2-(2,4,6-trimethylphenyl)sulfonylaminobenzylthio]imidazole in 2 ml of dimethyl formamide is added thereto under ice-cooling. The mixture is stirred at room temperature for 30 minutes, and 320 mg of methyl iodide are added thereto. The mixture is stirred for 2 hours. The reaction mixture

is poured into water, and the resultant oily product is extracted with ethyl acetate. The extract is dried and evaporated. The residue is purified by silica gel column chromatography (solvent; n-hexane : ethyl acetate = 3 : 2), whereby 0.76 g of 1-(2-pyridyl)-2-{2-[N-methyl-N-(2,4,6-trimethylphenyl)sulfonylamino]-benzylthio}imidazole is obtained.

M.p. 131 to 133 °C (recrystallized from ethyl acetate)

(2) The product obtained above is treated in the same manner as described in Example 71-(2) to give 1-(2-pyridyl)-2-(2-methylaminobenzylthio)imidazole as an oil.

Yield 92%

Mass(m/e):296(M^+), 120

^{1}H-NMR($CDCl_3$,δ):2.83(d,3H,J = 3Hz,NCH_3),4.42(s,2H,SCH_2), 5.20(br,1H,NH)

(3) The product obtained above is treated in the same manner as described in Example 1-(2) to give 1-(2-pyridyl)-2-(2-methylaminobenzylsulfinyl)imidazole.

M.p. 135 to 137 °C (recrystallized from ethyl acetate)

Example 77

(1) 1-(2-pyridylmethyl)-2-mercaptoimidazole and 2-phthalimidobenzyl chloride are treated in the same manner as described in Example 1-(1) to give 1-(2-pyridylmethyl)-2-(2-phthalimidobenzylthio)imidazole.

M.p. 80 to 83 °C (recrystallized from ethanol)

(2) The product obtained above is treated in the same manner as described in Example 75-(2) to give 1-(2-pyridylmethyl)-2-(2-aminobenzylthio)imidazole as an oil.

Mass(m/e):296(M^+), 106

^{1}H-NMR($CDCl_3$,δ):4.21(s,2H,SCH_2),4.31(br,2H,NH_2), 5.10(s,2H,NCH_2)

(3) The product obtained above is treated in the same manner as described in Example 1-(2) to give 1-(2-pyridylmethyl)-2-(2-aminobenzylsulfinyl)imidazole.

Mass(m/e):312(M^+), 106

^{1}H-NMR($CDCl_3$,δ):4.26(br,2H,NH_2),4.59(ABq,2H,NCH_2), 5.29(ABq,2H,NCH_2)

Example 101

(1) 3.26 g of 1-(3-hydroxy-2-pyridyl)-2-(2-dimethylaminobenzylthio)imidazole are dissolved in 100 ml of dimethyl formamide, and 0.48 g of 60% sodium hydride is added thereto. After the mixture is stirred for 20 minutes, 1.3 ml of isopropyl bromide are added dropwised thereto, and the mixture is further stirred at room temperature for 17 hours. The reaction mixture is poured into ice water, extracted with ethyl acetate, dried and evaporated to remove the solvent. The residue is recrystallized from a mixture of ethyl acetate and n-hexane, whereby 2.47 g of 1-(3-isopropoxy-2-pyridyl)-2-(2-dimethylaminobenzylthio)-imidazole are obtained.

Yield 67%

M.p. 85 to 87 °C

(2) The product obtained above is treated in the same manner as described in Example 1-(2) to give 1-(3-isopropoxy-2-pyridyl)-2-(2-dimethylaminobenzylsulfinyl)imidazole.

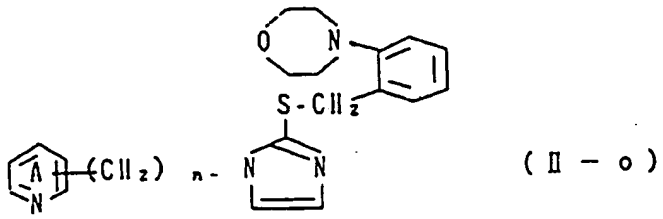
Mass(m/e):384(M^+), 134

^{1}H-NMR($CDCl_3$,δ): 1.32 and 1.34 (d, 3H, CH_3, respectively), 2.63(s,6H,$N(CH_3)_2$),4.81(ABq,2H,SCH_2)

Examples 102

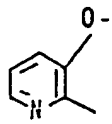
(1) The corresponding starting compounds are treated in the same manner as described in Example 101-(1) to give the compounds shown in Table 23.

Table 23



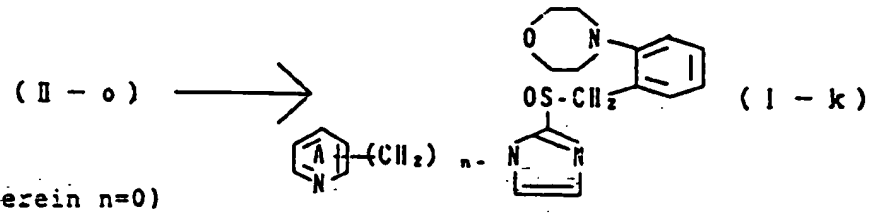
(II - o)

(wherein n=0)

Ex. Nos.	Compound(II-o) Ring A	Properties
102 -(1)		M.p. 117 to 119 °C(recrystallized from ethyl acetate and n-hexane)

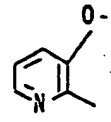
(2) The product obtained above is treated in the same manner as described in Example 1-(2) to give the compound shown in Table 24.

Table 24



(I - k)

(wherein n=0)

Ex. Nos.	Compound(I-k) Ring A	Properties*)
102 -(2)		M.p. 120 to 122 °C(recrystallized from ethyl acetate and n-hexane)

*) note: NMR is measured in $CDCl_3$

[Preparation of starting compounds]

Preparation 1

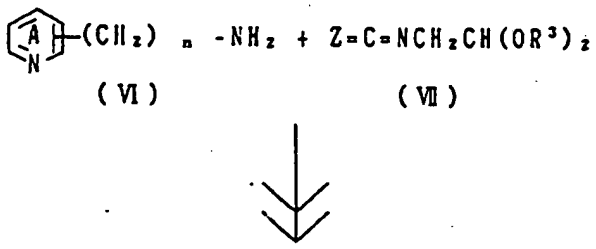
(1) A solution of 3.76 g of 2-aminopyridine and 7 g of 2,2-diethoxyethyl isothiocyanate in toluene is refluxed. After the reaction, the solvent is distilled off, and the residue is recrystallized from a mixture of ethyl acetate and n-hexane, whereby 9 g of N-(2,2-diethoxyethyl)-N'-(2-pyridyl)thiourea are obtained.
M.p. 126 to 128 °C

(2) A solution of 8.94 g of the product obtained above and a small amount of conc. hydrochloric acid in acetic acid is refluxed. After the reaction, the solution is evaporated to remove the solvent. The residue is dissolved in water, and sodium bicarbonate is added thereto. The crystalline precipitates are collected by filtration, whereby 4.91 g of 1-(2-pyridyl)-2-mercaptoimidazole are obtained.
M.p. 159 to 161 °C (recrystallized from isopropyl alcohol, isopropyl ether and n-hexane)

Preparations 2 to 25

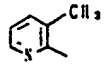
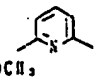
The corresponding starting compounds are treated in the same manner as described in Preparation 1-(1) and (2) to give the compounds shown in Table 25.

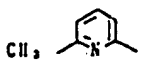
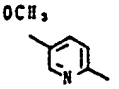
Table 25



(wherein n=1 in Pr. No. 2, n=0 in Pr. Nos. 3 to 24, and n=2 in Pr. No. 25, R^1 and R^2 are hydrogen atom, R^3 is ethyl, and Z is sulfur atom)

Pr. Nos.	Compound(III) Ring A	Properties
2		M.p. 181 to 183 °C(recrystallized from ethanol)
3		M.p. 209.5 to 211.5 °C(recrystallized from methanol)

6		M.p. 223 to 225 °C(recrystallized from ethanol)
7		M.p. 187 to 190 °C(recrystallized from ethanol)
9		M.p. 188 to 190 °C(recrystallized from ethanol)
10		M.p. 166 to 168 °C(recrystallized from ethanol)
17		M.p. 208 to 211 °C(recrystallized

		from ethyl acetate)
13		M.p. 263 to 265 °C(recrystallized from ethanol)
20		M.p. 157 to 159 °C(recrystallized from methanol)
21		M.p. about 185 °C(decomp. recrystallized from ethanol)
22		M.p. 158 to 160 °C(recrystallized from ethanol)
25		M.p. 161 to 163.5 °C(recrystallized from ethanol)

Preparation 26

(1) A solution of 57.96 g of o-dimethylcarbamoylbenzoic acid in tetrahydrofuran is added dropwise to a tetrahydrofuran suspension of 34.05 g of sodium borohydride. After the reaction at room temperature, 170.3 g of boron trifluoride etherate are added dropwise thereto, and the mixture is further refluxed. After cooling, a solution of 54 g of oxalic acid in water and methanol is added thereto, and the mixture is further refluxed. The reaction mixture is condensed and extracted with ethyl acetate under an alkaline condition. The extract is evaporated to remove the solvent, and the residue is distilled under reduced pressure, whereby 19.04 g of o-dimethylaminomethylbenzyl alcohol are obtained.
B.p. 106 to 109 °C (4mmHg)
(2) 2.89 g of thionyl chloride are added dropwise to a methylene chloride solution of 2.9 g of the product obtained above. After the reaction at room temperature, the mixture is diluted with ether. The crystalline

precipitates are collected by filtration, whereby 3.78 g of o-dimethylaminomethylbenzylchloride hydrochloride are obtained.
M.p. 143 to 147 °C

Preparation 27

(1) To a tetrahydrofuran solution of 5.12 g of N-phenylanthranilic acid, 32.2 ml of a hexane solution of n-butyl lithium and a solution of 4.42 g of methyl iodide in tetrahydrofuran are added successively at -60 °C and the mixture is reacted at room temperature. After the reaction, water is added thereto, and the aqueous mixture is extracted with ethyl acetate under an acidic condition. The extract is evaporated to remove the solvent, whereby 5.06 g of N-methyl-N-phenyl anthranilic acid are obtained as an oil.
Yield 93%
Mass(m/e):227(M^+)
^{1}H-NMR($CDCl_3$,δ): 3.22(s,3H,NCH_3)

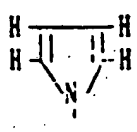
liquid
IR ν_{max} (cm^{-1}): 1690 (COOH)

(2) A solution of 5.06 g of N-methyl-N-phenyl anthranilic acid in tetrahydrofuran is added dropwise to a tetrahydrofuran suspension of 1.7 g of lithium alminum hydride under ice-cooling. After the reaction at room temperature, the mixture is cooled in an ice bath. Water and a saturated aqueous sodium sulfate solution are added to the mixture, and insoluble materials are filtered off. The filtrate is evaporated to remove the solvent, and the residue is purified by silica gel column chromatography, whereby 4.33 g of o-N-methyl-N- phenylaminobenzyl alcohol are obtained as a colorless oil.
Mass(m/e):213(M^+)
^{1}H-NMR($CDCl_3$,δ): 2.10(t,1H,J = 6Hz,OH),3.21(s,3H,NCH_3), 4.56(d,2H,J = 6Hz,CH_2O)

liquid
IR ν_{max} (cm^{-1}): 3360

Preparation 28

A solution of 9 g of ethyl o-(1-pyrrolyl)benzoate in ether is added dropwise to an ether suspension of 2.4 g of lithium alminum hydride under ice-cooling. After the reaction, water and a saturated aqueous sodium sulfate solution are added to the mixture, and insoluble materials are filtered off. The filtrate is evaporated to remove the solvent, and the residue is distilled under reduced pressure, whereby 6.3 g of o-(1-pyrrolyl)benzyl alcohol are obtained.
B.p. 120 to 135 °C(3 to 4 mmHg
Mass(m/e):173(M^+)
^{1}H-NMR($CDCl_3$,δ): 4.52(s,2H,CH_2O), 6.30 and 6.83

(respectively, t,2H,J=2Hz, )

liquid
IR ν_{max} (cm^{-1}): 3380

Preparation 29

A mixture of 6.82 g of 2-aminocyclohexanone hydrochloride, 6.21 g of 2-pyridylisothiocyanate dimer and 100 ml of toluene is stirred under heating. When the temperature is cooled down to 50 °C, 4.61 g of triethylamine are added dropwise thereto. after the reaction, water is added to the reaction mixture, and the aqueous mixture is extracted with ethyl acetate. The extract is washed with a saturated sodium chloride solution, dried and evaporated to remove the solvent, whereby 8.2 g of N-(2-pyridyl)-N'-(2-oxocyclohexyl)-thiourea are obtained.

Yield 72%

M.p. 149 to 151 °C

Preparation 30

2-aminocyclopentanone hydrochloride is treated in the same manner as described in Preparation 29 to give 2-mercapto-1,3a,4,5,6,6a-hexahydro-6a-hydroxy-1-(2-pyridil)cyclopenta[d]imidazole.

Yield 55%

M.p. 126 to 127 °C

Preparation 31

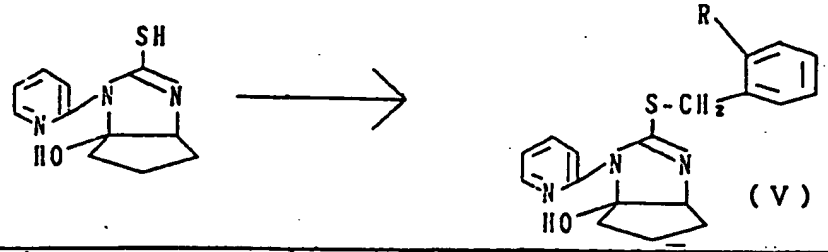
N-(2-pyridyl)-N'-(2-oxocyclohexyl)thiourea is treated in the same manner as described in Example 67-(1) to give 1-(2-pyridyl)-4,5,6,7-tetrahydrobenzimidazol-2-thione.

M.p. 203 to 204 °C (recrystallized from ethyl acetate and n-hexane)

Preparations 32 to 36

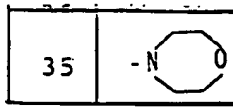
2-mercapto-1,3a,4,5,6,6a-hexahydro-6a-hydroxy-1-(2-pyridyl)cyclopenta[d]imidazole and the corresponding starting compounds are treated in the same manner as described in Example 1-(1) to give the compounds shown in Table 26.

Table 26



(V)

Pr. Nos.	compound(V) R	Properties
32	$-N(CH_3)_2$	oil
33	$-N(C_2H_5)_2$	oil

35		oil

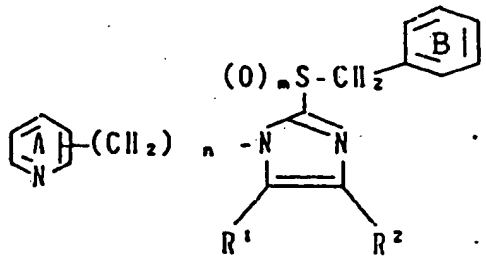
Preparation 37

(1) 24.2 g of ethyl o-fluorobenzoate and 9.8 g of imidazole are heated in the presence of sodium hydride, whereby 23 g of ethyl o-imidazolylbenzoate are obtained.
B.p. 165 to 167 °C (2 mmHg)
(2) 5 g of the product obtained above are treated in the same manner as described in Preparation 28 to give 3.4 g of o-imidazolylbenzyl alcohol.
(3) 3.4 g of the product obtained above are treated in the same manner as described in Preparation 26-(2) to give 3.3 g of o-imiazolylbenzyl chloride are obtained.
M.p. 160 to 161 °C (recrystallized from ethanol and ether)

Claims

Claims for the following Contracting States : AT, BE, CH, DE, GB, IT, LI, LU, NL, SE

1. An imidazole derivative of general formula:



(I)

wherein Ring A is a 2- or 4-pyridyl group or a 2- or 4-pyridyl group having a substituent selected from a C_{1-4} alkyl group and a C_{1-4} alkoxy group; Ring B is a phenyl group having one substituent selected from an amino group, a mono(C_{1-4} alkyl)amino group, a di(C_{1-4} alkyl)amino group, and a morpholino group; R^1 and R^2 are hydrogen atoms or are combined together to form a group of the formula: $-(CH_2)_q-$; m is 1; n is 0 or 1; and q is 3 or 4, or a pharmaceutically acceptable acid addition salt thereof.

2. A compound according to Claim 1, in which Ring A is a 2- or 4-pyridyl group, a 3-(C_{1-4} alkoxy)-2-pyridyl group or a 3- or 4-(C_{1-4} alkyl)-2-pyridyl group; and Ring B is a 2-morpholinophenyl group, a 2-aminophenyl group, a 2-mono(C_{1-4} alkyl)aminophenyl group or a 2-di(C_{1-4} alkyl)aminophenyl group.

3. A compound according to Claim 2, in which Ring A is a 2- or 4-pyridyl group, a 3-methoxy-2-pyridyl group or a 3- or 4-methyl-2-pyridyl group; and Ring B is a 2-morpholinophenyl group, a 2-aminophenyl group, a 2-methylaminophenyl group, a 2-ethylaminophenyl group, a 2-dimethylaminophenyl group or a 2-diethylaminophenyl group.

4. A compound according to Claim 1, wherein Ring A is a (C_{1-4} alkyl)-2-pyridyl group; Ring B is a phenyl group having one substituent selected from an amino group, a mono(C_{1-4} alkyl)amino group, a di(C_{1-4} alkyl) amino group; R^1 and R^2 are hydrogen atoms or are combined together to form a trimethylene group; and n is 0.

5. A compound according to Claim 4, wherein Ring A is a 3-(C_{1-4} alkyl)-2-pyridyl group; and Ring B is a 2-aminophenyl group, a 2-mono-(C_{1-4} alkyl)aminophenyl group or a 2-di(C_{1-4} alkyl)aminophenyl group.

6. A compound according to Claim 5, wherein Ring A is a 3-methyl-2-pyridyl group; and Ring B is a 2-aminophenyl group, a 2-methylaminophenyl group or a 2-dimethylaminophenyl group.

7. A compound according to Claim 5, in which Ring B is a 2-di(C_{1-4} alkyl)aminophenyl group.

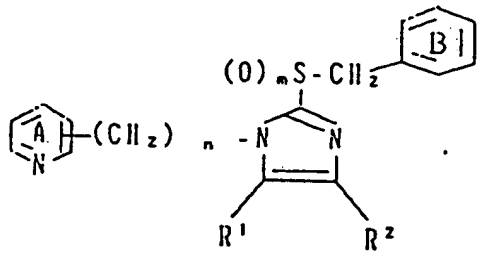
8. A compound according to Claim 6 in which Ring B is 2-dimethylaminophenyl group and R^1 and R^2 are combined together to form a trimethylene group.

9. A compound according to Claim 6, which is 1-(3-methyl-2-pyridyl)-2-[2-(dimethylamino)benzylsulfinyl]-imidazoleor a pharmaceutically acceptable acid addition salt thereof.

10. A compound according to any preceding claim for use in a method of therapy.

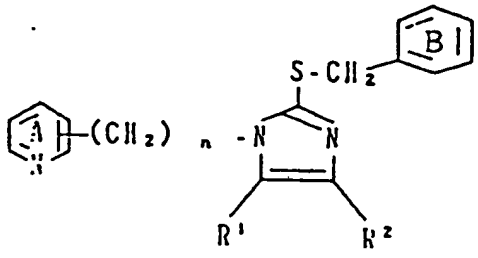
11. A compound according to any of claims 1-9 for use in the treatment or prevention of ulcers.

12. A process for the preparation of an imidazole derivative of the formula:



(I)

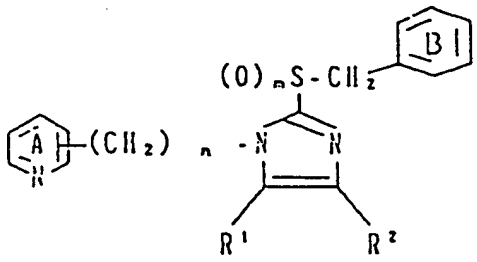
wherein Ring A is a 2- or 4-pyridyl group or a 2- or 4-pyridyl group having a substituent selected from a C_{1-4} alkyl group and a C_{1-4} alkoxy group; Ring B is a phenyl group having one substituent selected from an amino group, a mono(C_{1-4} alkyl)amino group, a di(C_{1-4} alkyl)amino group, and a morpholino group; R^1 and R^2 are hydrogen atoms or are combined together to form a group of the formula: $-(CH_2)_q-$; m is 1; n is 0 or 1; and q is 3 or 4, or a sale thereof, which comprises oxidizing an imidazole derivative of the formula:



(II)

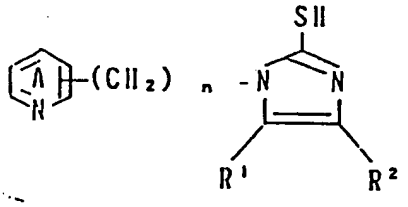
wherein Ring A, Ring B, R^1, R^2 and n are the same as defined above, or a salt thereof, and, if required, further converting the product into a salt thereof.

13. A process for the preparation of an imidazole derivative of the formula:



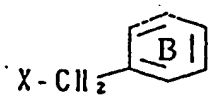
(I)

wherein Ring A is a 2- or 4-pyridyl group or a 2- or 4-pyridyl group having a substituent selected from a C_{1-4} alkyl group and a C_{1-4} alkoxy group; Ring B is a phenyl group having one substituent selected from an amino group, a mono(C_{1-4} alkyl)amino group, a di(C_{1-4} alkyl)amino group, and a morpholino group; R^1 and R^2 are hydrogen atoms or are combined together to form a group of the formula: $-(CH_2)_q-$; m is 1; n is 0 or 1; and q is 3 or 4, or a salt thereof, which comprises the steps of:
condensing a mercaptoimidazole compound of the formula:



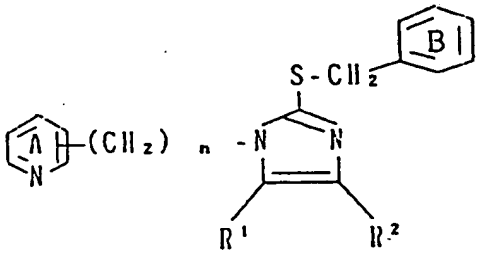
(III)

wherein Ring A, R^1, R^2 and n are the same as defined above, or a salt thereof with a toluene compound of the formula:



(IV)

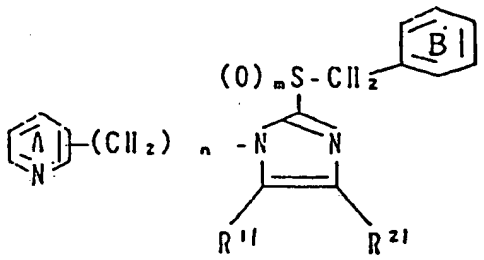
wherein X is a reactive residue, and Ring B is the same as defined above, or a salt thereof,
oxidizing the resultant product of the formula:



(II)

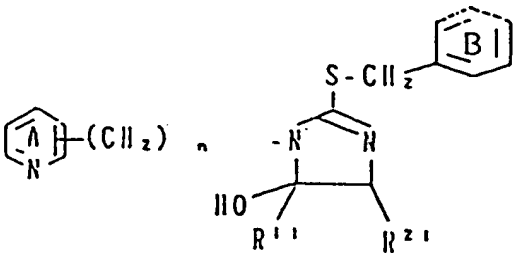
wherein Ring A, Ring B, R^1, R^2 and n are the same as defined above, and if required, further converting the product into a salt thereof.

14. A process for the preparation of an imidazole derivative of the formula:



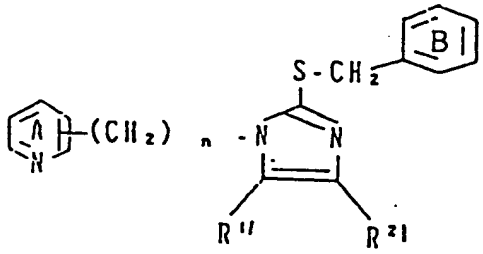
(I)

wherein Ring A is a 2- or 4-pyridyl group or a 2- or 4-pyridyl group having a substituent selected from a C_{1-4} alkyl group and a C_{1-4} alkoxy group; Ring B is a phenyl group having one substituent selected from an amino group, a mono(C_{1-4} alkyl)amino group, a di(C_{1-4} alkyl)amino group, and a morpholino group; R^{11} and R^{21} are combined together to form a group of the formula: $-(CH_2)_q-$; m is 1; n is 0 or 1; and q is 3 or 4, or a salt thereof, which comprises the steps of:
dehydrating a compound of the formula:



(V)

wherein R^{11}, R^{21}, Ring A, Ring B, and n are the same as defined above,
oxidizing the resultant product of the formula:



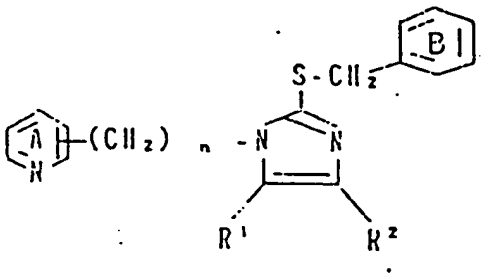
(II)

wherein Ring A, Ring B, R^{11}, R^{21} and n are the same as defined above, and if required, further converting the product into a salt thereof.

15. A pharmaceutical composition which comprises a pharmaceutically effective amount of a compound according to any of claims 1-9 and a pharmaceutically acceptable carrier.

16. The use of a compound according to any of claims 1-9 for the manufacture of a medicament for the treatment or prevention of ulcers.

17. An imidazole derivative of the formula:

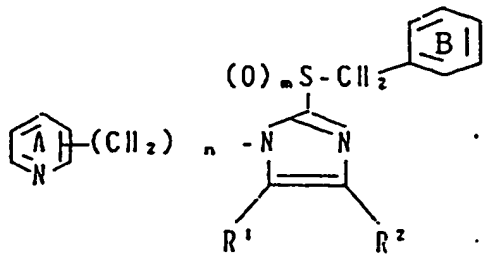


(II)

wherein Ring A is a 2- or 4-pyridyl group or a 2- or 4-pyridyl group having a substituent selected from a C_{1-4} alkyl group and a C_{1-4} alkoxy group; Ring B is a phenyl group having one substituent selected from an amino group, a mono(C_{1-4} alkyl)amino group, a di(C_{1-4} alkyl)amino group, and a morpholino group; R^1 and R^2 are hydrogen atoms or are combined together to form a group of the formula: $-(CH_2)_q-$; n is 0 or 1; and q is 3 or 4, or a salt thereof.

Claims for the following Contracting States : ES, GR

1. The use of an imidazole derivative of general formula:



(I)

wherein Ring A is a 2- or 4-pyridyl group or a 2- or 4-pyridyl group having a substituent selected from a C_{1-4} alkyl group and a C_{1-4} alkoxy group; Ring B is a phenyl group having one substituent selected from an amino group, a mono(C_{1-4} alkyl)amino group, a di(C_{1-4} alkyl)amino group, and a morpholino group; R^1 and R^2 are hydrogen atoms or are combined together to form a group of the formula: $-(CH_2)_q-$; m is 1; n is 0 or 1; and q is 3 or 4, or a pharmaceutically acceptable acid addition salt thereof, for the manufacture of a medicament for the treatment or prevention of ulcers.

2. The use according to Claim 1, in which Ring A is a 2- or 4-pyridyl group, a 3-(C_{1-4} alkoxy)-2-pyridyl group or a 3- or 4-(C_{1-4} alkyl)-2-pyridyl group; and Ring B is a 2-morpholinophenyl group, a 2-aminophenyl group, a 2-mono(C_{1-4} alkyl)aminophenyl group or a 2-di(C_{1-4} alkyl)aminophenyl group.

3. The use according to Claim 2, in which Ring A is a 2- or 4-pyridyl group, a 3-methoxy-2-pyridyl group or a 3- or 4-methyl-2-pyridyl group; and Ring B is a 2-morpholinophenyl group, a 2-aminophenyl group, a 2-methylaminophenyl group, a 2-ethylaminophenyl group, a 2-dimethylaminophenyl group or a 2-diethylaminophenyl group.

4. The use according to Claim 1, wherein Ring A is a (C_{1-4} alkyl)-2-pyridyl group; Ring B is a phenyl group having one substituent selected from an amino group, a mono(C_{1-4} alkyl)amino group, a di(C_{1-4} alkyl) amino group; R^1 and R^2 are hydrogen atoms or are combined together to form a trimethylene group; and n is 0.

5. The use according to Claim 4, wherein Ring A is a 3-(C_{1-4} alkyl)-2-pyridyl group; and Ring B is a 2-aminophenyl group, a 2-mono-(C_{1-4} alkyl)aminophenyl group or a 2-di(C_{1-4} alkyl)aminophenyl group.

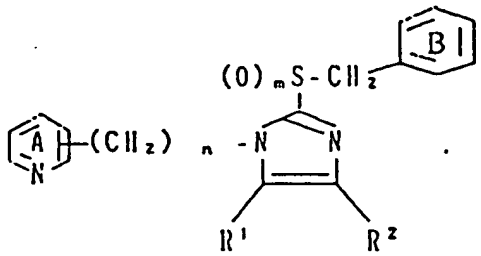
6. The use according to Claim 5, wherein Ring A is a 3-methyl-2-pyridyl group; and Ring B is a 2-aminophenyl group, a 2-methylaminophenyl group or a 2-dimethylaminophenyl group.

7. The use according to Claim 5, in which Ring B is a 2-di(C_{1-4} alkyl)aminophenyl group.

8. The use according to Claim 6 in which Ring B is 2-dimethylaminophenyl group and R^1 and R^2 are combined together to form a trimethylene group.

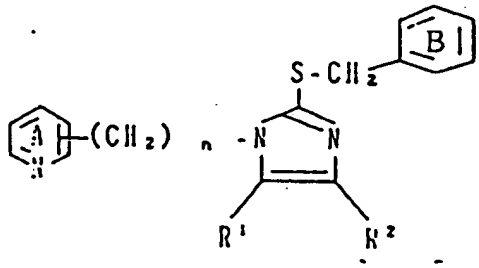
9. The use according to Claim 6, wherein the imidazole derivative is 1-(3-methyl-2-pyridyl)-2-[2-(dimethylamino)- benzylsulfinyl]imidazole or a pharmaceutically acceptable acid addition salt thereof.

10. A process for the preparation of an imidazole derivative of the formula:



(I)

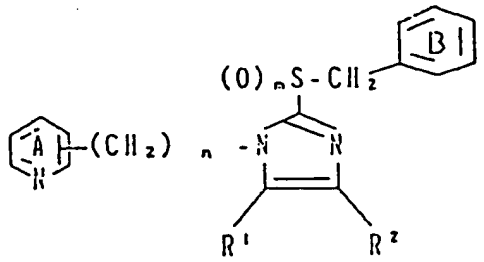
wherein Ring A is a 2- or 4-pyridyl group or a 2- or 4-pyridyl group having a substituent selected from a C_{1-4} alkyl group and a C_{1-4} alkoxy group; Ring B is a phenyl group having one substituent selected from an amino group, a mono(C_{1-4} alkyl)amino group, a di(C_{1-4} alkyl)amino group, and a morpholino group; R^1 and R^2 are hydrogen atoms or are combined together to form a group of the formula: $-(CH_2)_q-$; m is 1; n is 0 or 1; and q is 3 or 4, or a salt thereof, which comprises oxidizing an imidazole derivative of the formula:



(II)

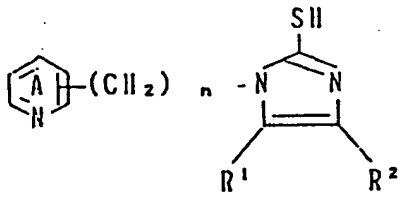
wherein Ring A, Ring B, R^1, R^2 and n are the same as defined above, or a salt thereof, and, if required, further converting the product into a salt thereof.

11. A process for the preparation of an imidazole derivative of the formula:



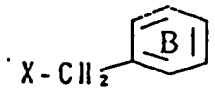
(I)

wherein Ring A is a 2- or 4-pyridyl group or a 2- or 4-pyridyl group having a substituent selected from a C_{1-4} alkyl group and a C_{1-4} alkoxy group; Ring B is a phenyl group having one substituent selected from an amino group, a mono(C_{1-4} alkyl)amino group, a di(C_{1-4} alkyl)amino group, and a morpholino group; R^1 and R^2 are hydrogen atoms or are combined together to form a group of the formula: $-(CH_2)_q-$; m is 1; n is 0 or 1; and q is 3 or 4, or a salt thereof, which comprises the steps of:
condensing a mercaptoimidazole compound of the formula:



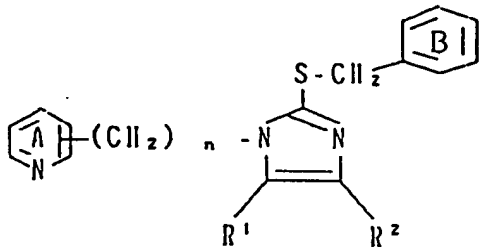
(III)

wherein Ring A, R^1, R^2 and n are the same as defined above, or a salt thereof with a toluene compound of the formula:



(IV)

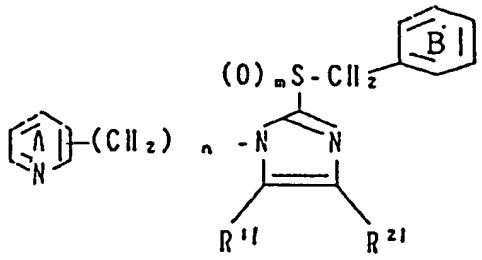
wherein X is a reactive residue, and Ring B is the same as defined above, or a salt thereof,
oxidizing the resultant product of the formula:



(II)

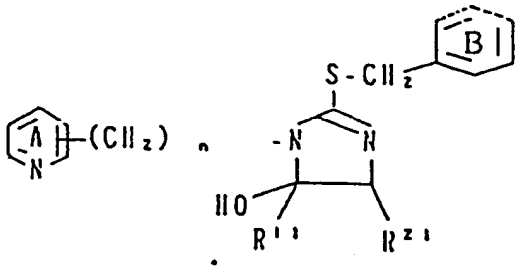
wherein Ring A, Ring B, R^1, R^2 and n are the same as defined above, and if required, further converting the product into a salt thereof.

12. A process for the preparation of an imidazole derivative of the formula:



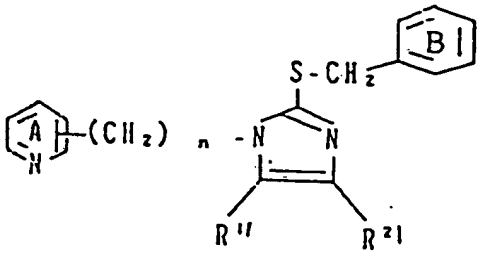
(I)

wherein Ring A is a 2- or 4-pyridyl group or a 2- or 4-pyridyl group having a substituent selected from a C_{1-4} alkyl group and a C_{1-4} alkoxy group; Ring B is a phenyl group having one substituent selected from an amino group, a mono(C_{1-4} alkyl)amino group, a di(C_{1-4} alkyl)amino group, and a morpholino group; R^{11} and R^{21} are combined together to form a group of the formula: $-(CH_2)_q-$; m is 1; n is 0 or 1; and q is 3 or 4, or a salt thereof, which comprises the steps of:
dehydrating a compound of the formula:



(V)

wherein R^{11}, R^{21}, Ring A, Ring B, and n are the same as defined above,
oxidizing the resultant product of the formula:

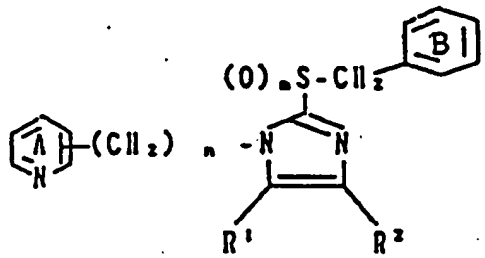


(II)

wherein Ring A, Ring B, R^{11}, R^{21} and n are the same as defined above, and if required, further converting the product into a salt thereof.

Patentansprüche
Patentansprüche für folgende Vertragsstaaten : AT, BE, CH, DE, GB, IT, LI, LU, NL, SE

1. Imidazolderivat der allgemeinen Formel



(I)

worin der Ring A eine 2- oder 4-Pyridylgruppe ist oder eine 2- oder 4-Pyridylgruppe mit einem Substituenten, ausgewählt unter einer C_1-C_4-Alkylgruppe und einer C_1-C_4-Alkoxygruppe; der Ring B ist eine Phenylgruppe mit einem Substituenten, ausgewählt aus einer Aminogruppe, einer Mono(C_1-C_4-alkyl)aminogruppe, einer Di(C_1-C_4-alkyl)-aminogruppe und einer Morpholingruppe; R^1 und R^2 sind Wasserstoffatome oder sind miteinander kombiniert, daß sie eine Gruppe der Formel $-(CH_2)_q-$ bilden; m ist 1; n ist 0 oder 1; und q ist 3 oder 4; oder ein pharmazeutisch annehmbares Säureadditionssalz davon.

2. Verbindung nach Anspruch 1, worin der Ring A eine 2- oder 4-Pyridylgruppe, eine 3-(C_1-C_4-Alkoxy)-2-pyridylgruppe oder eine 4-(C_1-C_4-Alkyl)-2-pyridylgruppe ist; und der Ring B ist eine 2-Morpholinphenylgruppe, eine 2-Aminophenylgruppe, eine 2-Mono(C_1-C_4-alkyl)-aminophenylgruppe oder eine 2-Di(C_1-C_4-alkyl)-aminophenylgruppe.

3. Verbindung nach Anspruch 2, worin der Ring A eine 2- oder 4-Pyridylgruppe , eine 3-Methoxy-2-pyridylgruppe oder eine 3- oder 4-Methyl-2-pyridylgruppe ist; und der Ring B ist eine 2-Morpholinphenylgruppe, eine 2-Aminophenylgruppe, eine 2-Methylaminophenylgruppe, eine 2-Ethylaminophenylgruppe, eine 2-Dimethylaminophenylgruppe oder eine 2-Diethylaminophenylgruppe.

4. Verbindung nach Anspruch 1, worin der Ring A eine (C_1-C_4-Alkyl)-2-pyridylgruppe ist; der Ring B ist eine Phenylgruppe mit einem Substituenten, ausgewählt aus einer Aminogruppe, einer Mono(C_1-C_4-alkyl)aminogruppe, einer Di(C_1-C_4-alkyl)aminogruppe; R^1 und R^2 sind Wasserstoffatome oder miteinander kombiniert, so daß sie eine Trimethylengruppe bilden; und n ist 0.

5. Verbindung nach Anspruch 4, worin der Ring A eine 3-(C_1-C_4-Alkyl)-2-pyridylgruppe ist; und der Ring B ist eine 2-Aminophenylgruppe, eine 2-Mono-(C_1-C_4-alkyl)aminophenylgruppe oder eine 2-Di(C_1-C_4-alkyl)aminophenylgruppe.

6. Verbindung nach Anspruch 5, worin der Ring A eine 3-Methyl-2-pyridylgruppe ist; und der Ring B ist eine 2-Aminophenylgruppe, eine 2-Methylaminophenylgruppe oder eine 2-Dimethylaminophenylgruppe.

7. Verbindung nach Anspruch 5, worin der Ring B eine 2-Di(C_1-C_4-alkyl)aminophenylgruppe ist.

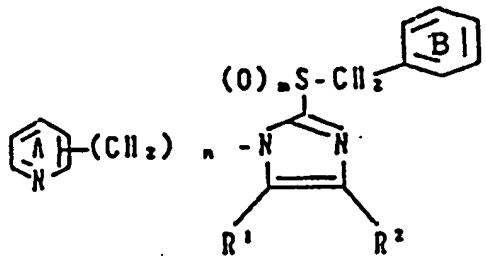
8. Verbindung nach Anspruch 6, worin der Ring B eine 2-Dimethylaminophenylgruppe ist und R^1 und R^2 miteinander kombiniert sind, so daß sie eine Trimethylengruppe bilden.

9. Verbindung nach Anspruch 6, worin diese 1-(3-Methyl-2-pyridyl)-2-[2-(dimethylamino)benzylsulfinyl]-imidazol oder ein pharmazeutisch annehmbares Säureadditionssalz davon ist.

10. Verbindung nach einem der vorherigen Ansprüche zur Verwendung in einem Verfahren zur Therapie.

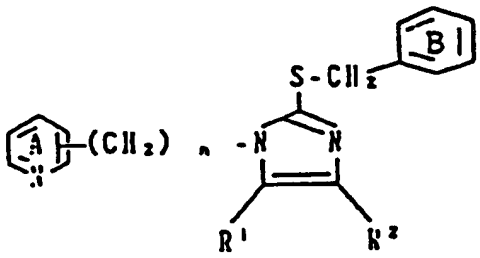
11. Verbindung nach einem der Ansprüche 1-9 zur Verwendung bei der Behandlung oder Verhütung von Ulceri.

12. Verfahren zur Herstellung eines Imidazolderivates der Formel



(I)

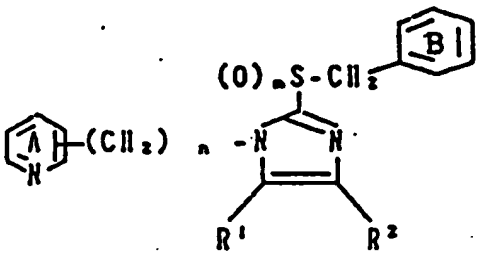
worin der Ring A eine 2- oder 4-Pyridylgruppe ist oder eine 2- oder 4-Pyridylgruppe mit einem Substituenten, ausgewählt unter einer C_1-C_4-Alkylgruppe und einer C_1-C_4-Alkoxygruppe; der Ring B ist eine Phenylgruppe mit einem Substituenten, ausgewählt aus einer Aminogruppe, einer Mono(C_1-C_4-alkyl)aminogruppe, einer Di(C_1-C_4-alkyl)-aminogruppe und einer Morpholingruppe; R^1 und R^2 sind Wasserstoffatome oder sind miteinander kombiniert, daß sie eine Gruppe der Formel $-(CH_2)_q-$ bilden; m ist 1; n ist 0 oder 1; und q ist 3 oder 4; oder ein Salz davon, gekennzeichnet durch Oxidieren eines Imidazolderivates der Formel



(II)

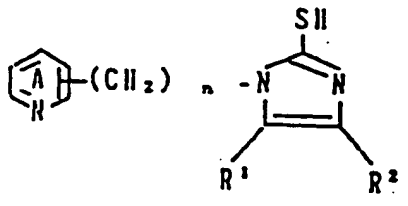
worin der Ring A, der Ring B, R^1, R^2 und n die oben definierte Bedeutung haben, oder ein Salz davon, und, falls gewünscht, weitere Umwandlung des Produktes in ein Salz davon.

13. Verfahren zur Herstellung eines Imidazolderivates der Formel



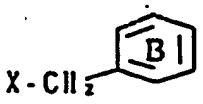
(I)

worin der Ring A eine 2- oder 4-Pyridylgruppe ist oder eine 2- oder 4-Pyridylgruppe mit einen Substituenten, ausgewählt unter einer C_1-C_4-Alkylgruppe und einer C_1-C_4-Alkoxygruppe; der Ring B ist eine Phenylgruppe mit einem Substituenten, ausgewählt aus einer Aminogruppe, einer Mono(C_1-C_4-alkyl)aminogruppe, einer Di(C_1-C_4-alkyl)-aminogruppe und einer Morpholingruppe; R^1 und R^2 sind Wasserstoffatome oder sind miteinander kombiniert, daß sie eine Gruppe der Formel $-(CH_2)_q-$ bilden; m ist 1; n ist 0 oder 1; und q ist 3 oder 4; oder ein Salz davon, gekennzeichnet durch die Stufen Kondensieren einer Mercaptoimidazolverbindung der Formel



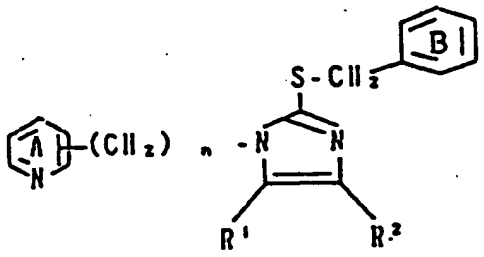
(III)

worin der Ring A, der Ring B, R^1, R^2 und n die oben definierte Bedeutung haben, oder ein Salz davon mit einer Toluenverbindung der Formel



(IV)

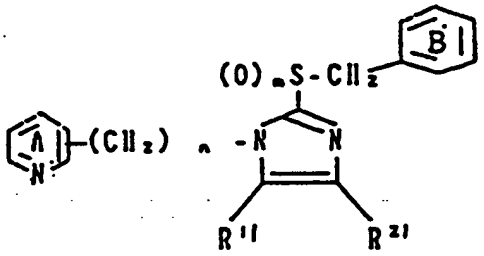
worin X ein reaktionsfähiger Rest ist und der Ring B die oben genannte Bedeutung hat, oder ein Salz davon,
Oxidieren des erhaltenen Produktes der Formel



(II)

worin der Ring A, der Ring B, R^1, R^2 und n die oben definierte Bedeutung haben, oder ein Salz davon, und, falls gewünscht, weitere Umwandlung des Produktes in ein Salz davon.

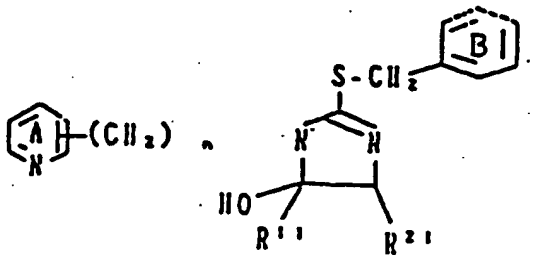
14. Verfahren zur Herstellung eines Imidazolderivates der Formel



(I')

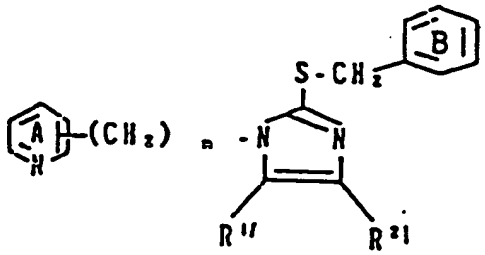
worin der Ring A eine 2- oder 4-Pyridylgruppe ist oder eine 2- oder 4-Pyridylgruppe mit einem Substituenten, ausgewählt unter einer C_1-C_4-Alkylgruppe und einer C_1-C_4-Alkoxygruppe; der Ring B ist eine Phenylgruppe mit einem Substituenten, ausgewählt aus einer Aminogruppe, einer Mono(C_1-C_4-alkyl)-aminogruppe, einer Di(C_1-C_4-alkyl)-aminogruppe und einer Morpholingruppe; R^{11} und R^{21} sind miteinander kombiniert, daß sie eine Gruppe der Formel $-(CH_2)_q-$ bilden; m ist 1; n ist 0 oder 1; und q

ist 3 oder 4; oder ein Salz davon,
gekennzeichnet durch die Stufen Dehydrieren einer Verbindung der Formel



(V)

worin R^{11}, R^{21}, der Ring A, der Ring B und n die gleiche Bedeutung wie oben haben,
Oxidieren des erhaltenen Produktes der Formel



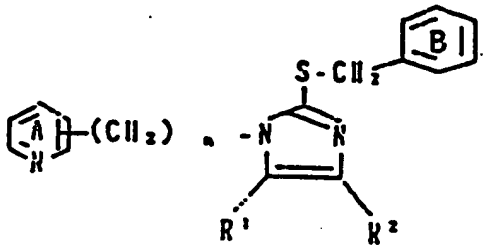
(II')

worin der Ring A, der Ring B, R^{11}, R^{21} und n die gleiche Bedeutung wie oben haben, und erforderlichenfalls weitere Umwandlung des Produktes in ein Salz davon.

15. Pharmazeutische Zusammensetzung, gekennzeichnet durch eine pharmazeutische wirksame Menge einer Verbindung nach einem der Ansprüche 1 - 9 und einen pharmazeutisch annehmbaren Träger.

16. Verwendung einer Verbindung nach einem der Ansprüche 1-9 zur Herstellung eines Medikamentes zur Behandlung oder Verhütung von Ulceri.

17. Imidazolderivat der Formel

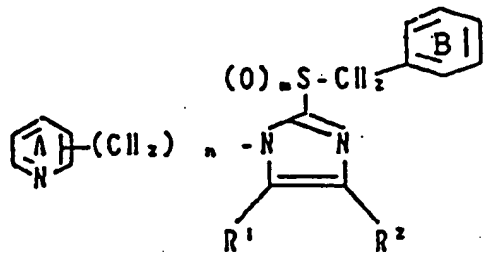


(II)

worin der Ring A eine 2- oder 4-Pyridylgruppe ist oder eine 2- oder 4-Pyridylgruppe mit einem Substituenten, ausgewählt unter einer C_1-C_4-Alkylgruppe und einer C_1-C_4-Alkoxygruppe; der Ring B ist eine Phenylgruppe mit einem Substituenten, ausgewählt aus einer Aminogruppe, einer Mono(C_1-C_4-alkyl)-aminogruppe, einer Di(C_1-C_4-alkyl)-aminogruppe und einer Morpholingruppe; R^1 und R^2 sind Wasserstoffatome oder sind miteinander kombiniert, daß sie eine Gruppe der Formel $-(CH_2)_q-$ bilden; n ist 0 oder 1; und q ist 3 oder 4; oder ein Salz davon.

Patentansprüche für folgende Vertragsstaaten : ES, GR

1. Verwendung eines Imidazolderivates der allgemeinen Formel



(I)

worin der Ring A eine 2- oder 4-Pyridylgruppe ist oder eine 2- oder 4-Pyridylgruppe mit einem Substituenten, ausgewählt unter einer C_1-C_4-Alkylgruppe und einer C_1-C_4-Alkoxygruppe; der Ring B ist eine Phenylgruppe mit einem Substituenten, ausgewählt aus einer Aminogruppe, einer Mono(C_1-C_4-alkyl)-aminogruppe, einer Di(C_1-C_4-alkyl)-aminogruppe und einer Morpholingruppe; R^1 und R^2 sind Wasserstoffatome oder sind miteinander kombiniert, daß sie eine Gruppe der Formel $-(CH_2)_q-$ bilden; m ist 1; n ist 0 oder 1; und q ist 3 oder 4; oder ein pharmazeutisch annehmbares Säureadditionssalz davon zur Herstellung eines Medikamentes zur Behandlung oder Verhütung von Ulceri.

2. Verwendung nach Anspruch 1, worin der Ring A eine 2- oder 4-Pyridylgruppe, eine 3-(C_1-C_4-Alkoxy)-2-Pyridylgruppe oder eine 4-(C_1-C_4-Alkyl)-2-Pyridylgruppe ist; und der Ring B ist eine 2-Morpholinphenylgruppe, eine 2-Aminophenylgruppe, eine 2-Mono(C_1-C_4-alkyl)-aminophenylgruppe oder eine 2-Di-(C_1-C_4-alkyl)-aminophenylgruppe.

3. Verwendung nach Anspruch 2, worin der Ring A eine 2- oder 4-Pyridylgruppe , eine 3-Methoxy-2-pyridylgruppe oder eine 3- oder 4-Methyl-2-pyridylgruppe ist; und der Ring B ist eine 2-Morpholinphenylgruppe, eine 2-Aminophenylgruppe, eine 2-Methylaminophenylgruppe, eine 2-Ethylaminophenylgruppe, eine 2-Dimethylaminophenylgruppe oder eine 2-Diethylaminophenylgruppe.

4. Verwendung nach Anspruch 1, worin der Ring A eine (C_1-C_4-Alkyl)-2-pyridylgruppe ist; der Ring B ist eine Phenylgruppe mit einem Substituenten, ausgewählt aus einer Aminogruppe, einer Mono(C_1-C_4-alkyl)aminogruppe, einer Di(C_1-C_4-alkyl)-aminogruppe; R^1 und R^2 sind Wasserstoffatome oder miteinander kombiniert, so daß sie eine Trimethylengruppe bilden; und n ist 0.

5. Verwendung nach Anspruch 4, worin der Ring A eine 3-(C_1-C_4-Alkyl)-2-pyridylgruppe ist; und der Ring B ist eine 2-Aminophenylgruppe, eine 2-Mono-(C_1-C_4-alkyl)aminophenylgruppe oder eine 2-Di(C_1-C_4-alkyl)aminophenylgruppe.

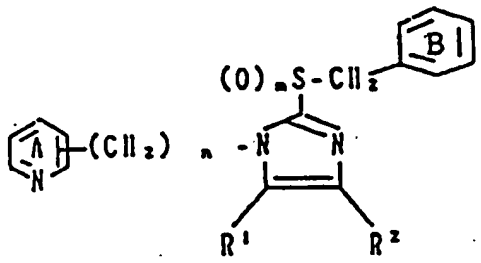
6. Verwendung nach Anspruch 5, worin der Ring A eine 3-Methyl-2-pyridylgruppe ist; und der Ring B ist eine 2-Aminophenylgruppe, eine 2-Methylaminophenylgruppe oder eine 2-Dimethylaminophenylgruppe.

7. Verwendung nach Anspruch 5, worin der Ring B eine 2-Di(C_1-C_4-alkyl)aminophenylgruppe ist.

8. Verwendung nach Anspruch 6, worin der Ring B eine 2-Dimethylaminophenylgruppe ist und R^1 und R^2 miteinander kombiniert sind, so daß sie eine Trimethylengruppe bilden.

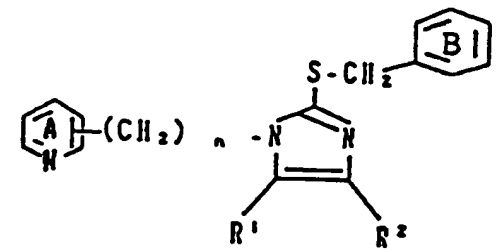
9. Verwendung nach Anspruch 6, worin diese 1-(3-Methyl-2-pyridyl)-2-[2-(dimethylamino)benzylsulfinyl]-imidazol oder ein pharmazeutisch annehmbares Säureadditionssalz davon ist.

10. Verfahren zur Herstellung eines Imidazolderivates der Formel



(I)

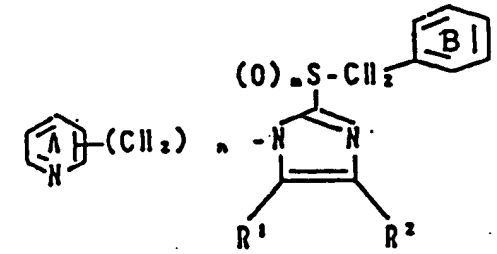
worin der Ring A eine 2- oder 4-Pyridylgruppe ist oder eine 2- oder 4-Pyridylgruppe mit einem Substituenten, ausgewählt unter einer C_1-C_4-Alkylgruppe und einer C_1-C_4-Alkoxygruppe; der Ring B ist eine Phenylgruppe mit einem Substituenten, ausgewählt aus einer Aminogruppe, einer Mono(C_1-C_4-alkyl)-aminogruppe, einer Di(C_1-C_4-alkyl)-aminogruppe und einer Morpholingruppe; R^1 und R^2 sind Wasserstoffatome oder sind miteinander kombiniert, daß sie eine Gruppe der Formel $-(CH_2)_q-$ bilden; m ist 1; n ist 0 oder 1; und q ist 3 oder 4; oder ein Salz davon, gekennzeichnet durch Oxidieren eines Imidazolderivates der Formel



(II)

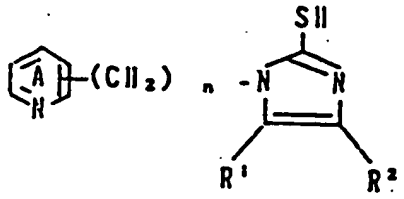
worin der Ring A, der Ring B, R^1 R^2 und n die oben definierte Bedeutung haben, oder ein Salz davon, und, falls gewünscht, weitere Umwandlung des Produktes in ein Salz davon.

11. Verfahren zur Herstellung eines Imidazolderivates der Formel



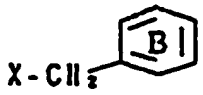
(I)

worin der Ring A eine 2- oder 4-Pyridylgruppe ist oder eine 2- oder 4-Pyridylgruppe mit einem Substituenten, ausgewählt unter einer C_1-C_4-Alkylgruppe und einer C_1-C_4-Alkoxygruppe; der Ring B ist eine Phenylgruppe mit einem Substituenten, ausgewählt aus einer Aminogruppe, einer Mono(C_1-C_4-alkyl)-aminogruppe, einer Di(C_1-C_4-alkyl)-aminogruppe und einer Morpholingruppe; R^1 und R^2 sind Wasserstoffatome oder sind miteinander kombiniert, daß sie eine Gruppe der Formel $-(CH_2)_q-$ bilden; m ist 1; n ist 0 oder 1; und q ist 3 oder 4; oder ein Satz davon, gekennzeichnet durch die Stufen Kondensieren einer Mercaptoimidazolverbindung der Formel



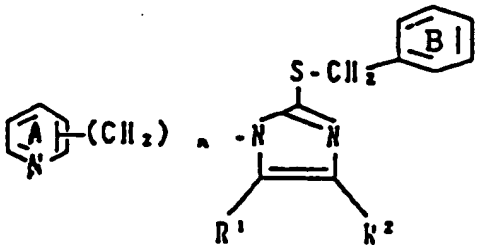
(III)

worin der Ring A, der Ring B, R^1, R^2 und n die oben definierte Bedeutung haben, oder ein Salz davon mit einer Toluenverbindung der Formel



(IV)

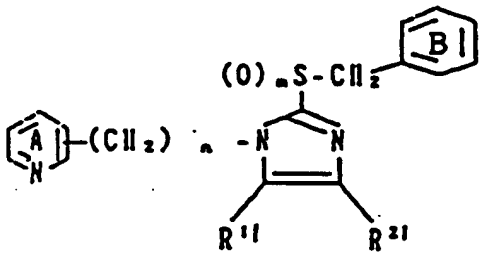
worin X ein reaktionsfähiger Rest ist und der Ring B die oben genannte Bedeutung hat, oder ein Salz davon,
Oxidieren des erhaltenen Produktes der Formel



(II)

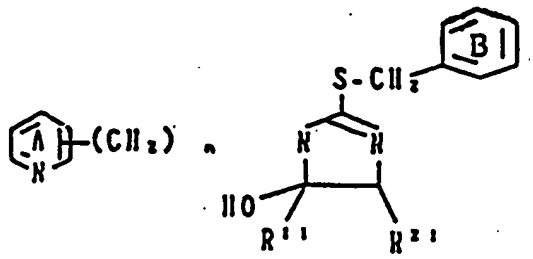
worin der Ring A, der Ring B, R^1, R^2 und n die oben definierte Bedeutung haben, oder ein Salz davon, und, falls gewünscht, weitere Umwandlung des Produktes in ein Salz davon.

12. Verfahren zur Herstellung eines Imidazolderivates der Formel



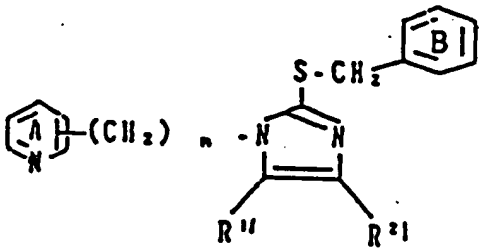
(I)

worin der Ring A eine 2- oder 4-Pyridylgruppe ist oder eine 2- oder 4-Pyridylgruppe mit einem Substituenten, ausgewählt unter einer C_1-C_4-Alkylgruppe und einer C_1-C_4-Alkoxygruppe; der Ring B ist eine Phenylgruppe mit einem Substituenten, ausgewählt aus einer Aminogruppe, einer Mono(C_1-C_4-alkyl)-aminogruppe, einer Di(C_1-C_4-alkyl)-aminogruppe und einer Morpholingruppe; R^{11} und R^{21} sind miteinander kombiniert, daß sie eine Gruppe der Formel $-(CH_2)_q-$ bilden; m ist 1; n ist 0 oder 1; und q ist 3 oder 4; oder ein Salz davon,
gekennzeichnet durch die Stufen Dehydrieren einer Verbindung der Formel



(V)

worin R^{11}, R^{21} der Ring A, der Ring B und n die gleiche Bedeutung wie oben haben,
Oxidieren des erhaltenen Produktes der Formel

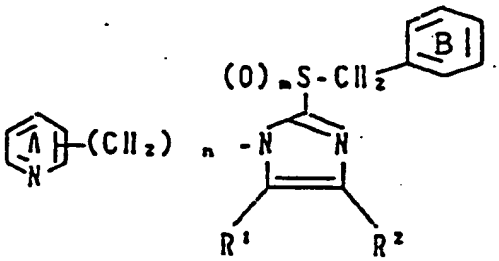


(II')

worin der Ring A, der Ring B, R^{11}, R^{21} und n die gleiche Bedeutung wie oben haben, und erforderlichenfalls weitere Umwandlung des Produktes in ein Salz davon.

Revendications
Revendications pour les Etats contractants suivants : AT, BE, CH, DE, GB, IT, LI, LU, NL, SE

1. Dérivé de l'imidazole répondant à la formule générale :



(I)

dans laquelle le Cycle A est un groupe 2- ou 4-pyridyle ou un groupe 2- ou 4-pyridyle ayant un substituant choisi parmi un groupe alkyle en C_1 à C_4 et un groupe alcoxy en C_1 à C_4; le Cycle B est un groupe phényle ayant un substituant choisi parmi un groupe amino, un groupe mono(alkyle en C_1 à C_4)amino, un groupe di(alkyle en C_1 à C_4)amino et un groupe morpholino; R^1 et R^2 sont des atomes d'hydrogène ou s'associent pour former un groupe répondant à la formule : $-(CH_2)_q-$; m est 1, n est 0 ou 1; et q est 3 ou 4, ou un de ses sels d'addition aux acides pharmaceutiquement acceptable.

2. Composé selon la revendication 1, dans lequel le Cycle A est un groupe 2- ou 4-pyridyle, un groupe 3-(alcoxy en C_1 à C_4)-2-pyridyle ou un groupe 3- ou 4-(alkyle en C_1 à C_4)-2-pyridyle; et le Cycle B est un groupe 2-morpholinophényle, un groupe 2-aminophényle, un groupe 2-mono(alkyle en C_1 à C_4)-

aminophényle ou un groupe 2-di(alkyle en C_1 à C_4)aminophényle.

3. Composé selon la revendication 2, dans lequel le Cycle A est un groupe 2- ou 4-pyridyle, un groupe 3-méthoxy-2-pyridyle ou un groupe 3- ou 4-méthyl-2-pyridyle; et le Cycle B est un groupe 2-morpholinophényle, un groupe 2-aminophényle, un groupe 2-méthylaminophényle, un groupe 2-éthylaminophényle, un groupe 2-diméthylaminophényle ou un groupe 2-diéthylaminophényle.

4. Composé selon la revendication 1, dans lequel le Cycle A est un groupe (alkyle en C_1 à C_4)-2-pyridyle; le Cycle B est un groupe phényle ayant un substituant choisi parmi un groupe amino, un groupe mono-(alkyle en C_1 à C_4)amino, un groupe di(alkyle en C_1 à C_4)amino; R^1 et R^2 sont des atomes d'hydrogène ou s'associent pour former un groupe triméthylène; et n est 0.

5. Composé selon la revendication 4, dans lequel le Cycle A est un groupe 3-(alkyle en C_1 à C_4)-2-pyridyle; et le Cycle B est un groupe 2-aminophényle, un groupe 2-mono-(alkyle en C_1 à C_4)-aminophényle ou un groupe 2-di(alkyle en C_1 à C_4)aminophényle.

6. Composé selon la revendication 5, dans lequel le Cycle A est un groupe 3-méthyl-2-pyridyle; et le Cycle B est un groupe 2-aminophényle, un groupe 2-méthylaminophényle ou un groupe 2-diméthylaminophényle.

7. Composé selon la revendication 5, dans lequel le Cycle B est un groupe 2-di(alkyle en C_1 à C_4)-aminophényle.

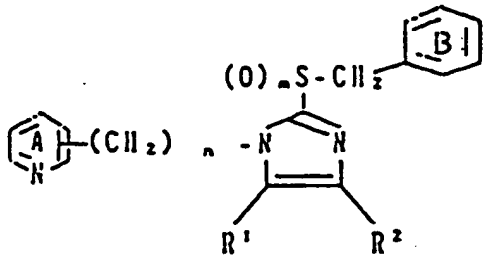
8. Composé selon la revendication 6, dans lequel le Cycle B est un groupe 2-diméthylaminophényle et R^1 et R^2 s'associent pour former un groupe triméthylène.

9. Composé selon la revendication 6, qui est le 1-(3-méthyl-2-pyridyle)-2-[2-(diméthylamino)-benzylsulfinyl]imidazole ou un de ses sels d'addition aux acides pharmaceutiquement acceptable.

10. Composé selon l'une quelconque des revendications précédentes, destiné à l'utilisation dans un procédé de traitement.

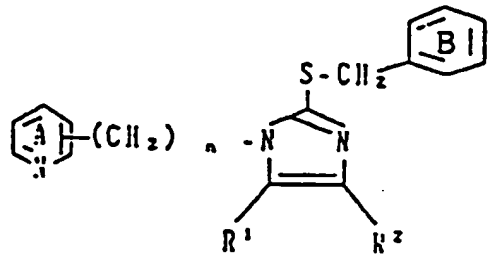
11. Composé selon l'une quelconque des revendications 1 à 9 destiné à l'utilisation pour le traitement ou la prévention des ulcères.

12. Procédé de préparation d'un dérivé de l'imidazole répondant à la formule :



(I)

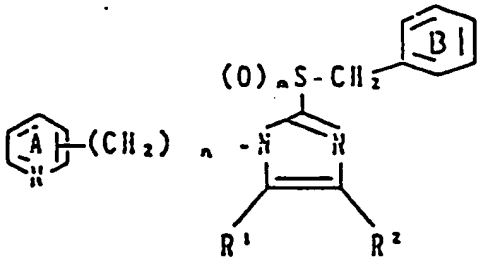
dans laquelle le Cycle A est un groupe 2- ou 4-pyridyle ou un groupe 2- ou 4-pyridyle ayant un substituant choisi parmi un groupe alkyle en C_1 à C_4 et un groupe alcoxy en C_1 à C_4; le Cycle B est un groupe phényle ayant un substituant choisi parmi un groupe amino, un groupe mono(alkyle en C_1 à C_4)amino, un groupe di(alkyle en C_1 à C_4)amino et un groupe morpholino; R^1 et R^2 sont des atomes d'hydrogène ou s'associent pour former un groupe répondant à la formule : $-(CH_2)_q-$; m est 1; n est 0 ou 1; et q est 3 ou 4, ou un de ses sels, qui comprend l'oxydation d'un dérivé de l'imidazole répondant à la formule :



(II)

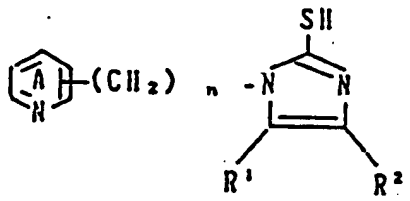
dans laquelle le Cycle A, le Cycle B, R^1, R^2 et n sont tels que définis ci-dessus, ou un de ses sels, et, si nécessaire, la transformation ultérieure du produit en l'un de ses sels.

13. Procédé de préparation d'un dérivé de l'imidazole répondant à la formule :



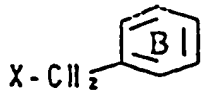
(I)

dans laquelle le Cycle A est un groupe 2- ou 4-pyridyle ou un groupe 2- ou 4-pyridyle ayant un substituant choisi parmi un groupe alkyle en C_1 à C_4 et un groupe alcoxy en C_1 à C_4; le Cycle B est un groupe phényle ayant un substituant choisi parmi un groupe amino, un groupe mono(alkyle en C_1 à C_4)amino, un groupe di(alkyle en C_1 à C_4)amino et un groupe morpholino; R^1 et R^2 sont des atomes d'hydrogène ou s'associent pour former un groupe répondant à la formule : $-(CH_2)_q-$; m est 1; n est 0 ou 1; et q est 3 ou 4, ou un de ses sels, qui comprend les stades consistant à :
condenser un mercaptoimidazole répondant à la formule :



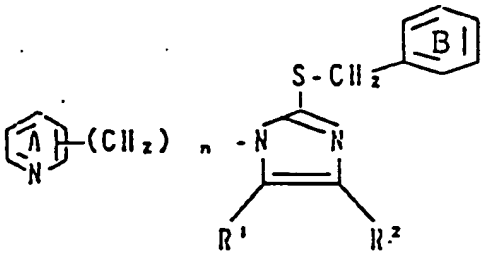
(III)

dans laquelle le Cycle A, R^1, et R^2 et n sont tels que définis ci-dessus, ou un de ses sels avec un dérivé du toluène répondant à la formule :



(IV)

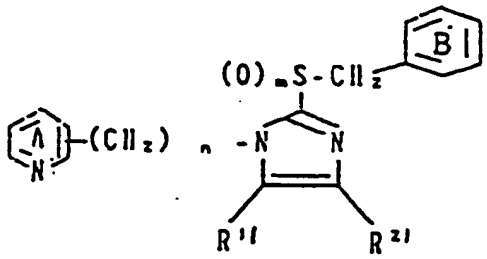
dans laquelle X est un radical réactif et le Cycle B est tel que défini ci-dessus, ou un de ses sels, oxyder le produit obtenu répondant à la formule :



(II)

dans laquelle le Cycle A, le Cycle B, R^1, R^2 et n sont tels que définis ci-dessus, et, si nécessaire, transformer ensuite le produit en l'un de ses sels.

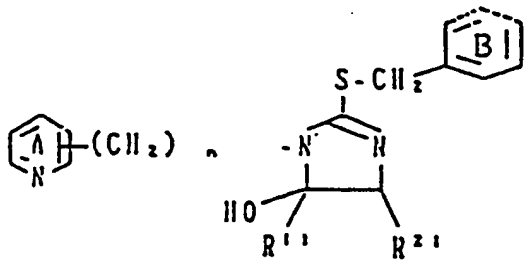
14. Procédé de préparation d'un dérivé de l'imidazole répondant à la formule :



(I')

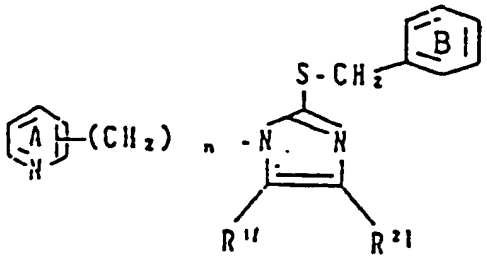
dans laquelle le Cycle A est un groupe 2- ou 4-pyridyle ou un groupe 2- ou 4-pyridyle ayant un substituant choisi parmi un groupe alkyle en C_1 à C_4 et un groupe alcoxy en C_1 à C_4; le Cycle B est un groupe phényle ayant un substituant choisi parmi un groupe amino, un groupe mono(alkyle en C_1 à C_4)amino, un groupe di(alkyle en C_1 à C_4)amino et un groupe morpholino; R^{11} et R^{21} s'associent pour former un groupe répondant à la formule: $-(CH_2)_q-$; m est 1; n est 0 ou 1; et q est 3 ou 4, ou un de ses sels, qui comprend les stades consistant à :

déshydrater un composé répondant à la formule :



(V)

dans laquelle R^{11}, R^{21}, le Cycle A, le Cycle B, et n sont tels que définis ci-dessus, oxyder le produit obtenu répondant à la formule :



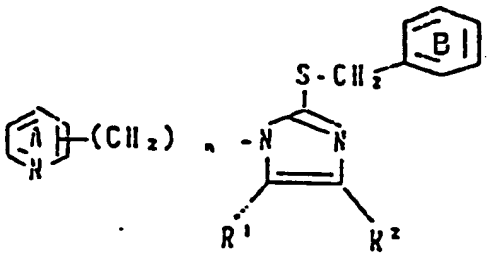
(II')

dans laquelle le Cycle A, le Cycle B, R^{11}, R^{21} et n sont tels que définis ci-dessus, et, si nécessaire, transformer ensuite le produit en l'un de ses sels.

15. Composition pharmaceutique qui comprend une quantité pharmaceutiquement efficace d'un composé selon l'une quelconque des revendications 1 à 9 et un support pharmaceutiquement acceptable.

16. Utilisation d'un composé selon l'une quelconque des revendications 1 à 9 pour la fabrication d'un médicament pour le traitement ou la prévention des ulcères.

17. Dérivé de l'imidazole répondant à la formule :

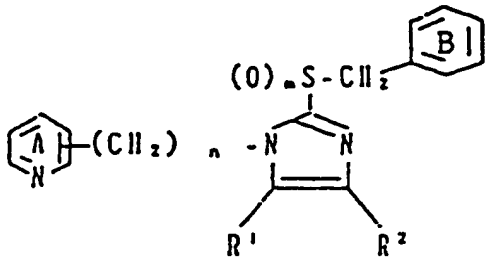


(II)

dans laquelle le Cycle A est un groupe 2- ou 4-pyridyle ou un groupe 2- ou 4-pyridyle ayant un substituant choisi parmi un groupe alkyle en C_1 à C_4 et un groupe alcoxy en C_1 à C_4; le Cycle B est un groupe phényle ayant un substituant choisi parmi un groupe amino, un groupe mono(alkyle en C_1 à C_4)amino, un groupe di(alkyle en C_1 à C_4)amino et un groupe morpholino; R^1 et R^2 sont des atomes d'hydrogène ou s'associent pour former un groupe répondant à la formule: $-(CH_2)_q-$; n est 0 ou 1; et q est 3 ou 4, ou un de ses sels.

Revendications pour les Etats contractants suivants : ES, GR

1. Utilisation d'un dérivé de l'imidazole répondant à la formule générale :



(I)

dans laquelle le Cycle A est un groupe 2- ou 4-pyridyle ou un groupe 2- ou 4-pyridyle ayant un substituant choisi parmi un groupe alkyle en C_1 à C_4 et un groupe alcoxy en C_1 à C_4; le Cycle B est un groupe phényle ayant un substituant choisi parmi un groupe amino, un groupe mono(alkyle en C_1 à C_4)amino, un groupe di(alkyle en C_1 à C_4)amino et un groupe morpholino; R^1 et R^2 sont des atomes d'hydrogène ou s'associent pour former un groupe répondant à la formule : $-(CH_2)_q-$; m est 1; n est 0 ou 1; et q est 3 ou 4, ou un de ses sels d'addition aux acides pharmaceutiquement acceptable, pour la fabrication d'un médicament pour le traitement ou la prévention des ulcères.

2. Utilisation selon la revendication 1, dans laquelle le Cycle A est un groupe 2- ou 4-pyridyle ou un groupe 3-(alcoxy en C_1 à C_4)-2-pyridyle ou un groupe 3- ou 4-(alkyle en C_1 à C_4)-2-pyridyle; et le Cycle B est un groupe 2-morpholinophényle, un groupe 2-aminophényle, un groupe 2-mono(alkyle en C_1 à C_4)aminophényle ou un groupe 2-di(alkyle en C_1 à C_4)aminophényle.

3. Utilisation selon la revendication 2, dans laquelle le Cycle A est un groupe 2- ou 4-pyridyle, un groupe 3-méthoxy-2-pyridyle ou un groupe 3- ou 4-méthyl-2-pyridyle; et le Cycle B est un groupe 2-morpholinophényle, un groupe 2-aminophényle, un groupe 2-méthylaminophényle, un groupe 2-éthylaminophényle, un groupe 2-diméthylaminophényle ou un groupe 2-diéthylaminophényle.

4. Utilisation selon la revendication 1, dans laquelle le Cycle A est un groupe (alkyle en C_1 à C_4)-2-pyridyle; le Cycle B est un groupe phényle ayant un substituant choisi parmi un groupe amino, un groupe mono(alkyle en C_1 à C_4)amino, un groupe di(alkyle en C_1 à C_4)amino; R^1 et R^2 sont des atomes d'hydrogène ou s'associent pour former un groupe triméthylène; et n est 0.

5. Utilisation selon la revendication 4, dans laquelle le Cycle A est un groupe 3-(alkyle en C_1 à C_4)-2-pyridyle; et le Cycle B est un groupe 2-aminophényle, un groupe 2-mono-(alkyle en C_1 à C_4)-aminophényle ou un groupe 2-di(alkyle en C_1 à C_4)aminophényle.

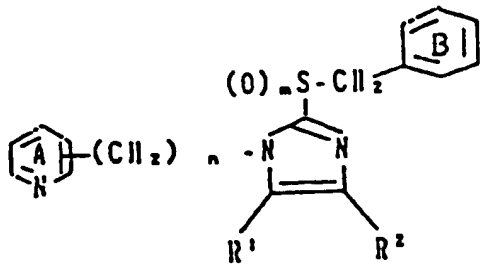
6. Utilisation selon la revendication 5, dans laquelle le Cycle A est un groupe 3-méthyl-2-pyridyle; et le Cycle B est un groupe 2-aminophényle, un groupe 2-méthylaminophényle ou un groupe 2-diméthylaminophényle.

7. Utilisation selon la revendication 5, dans laquelle le Cycle B est un groupe 2-di(alkyle en C_1 à C_4)-aminophényle.

8. Utilisation selon la revendication 6, dans laquelle le Cycle B est un groupe 2-diméthylaminophényle et R^1 et R^2 s'associent pour former un groupe triméthylène.

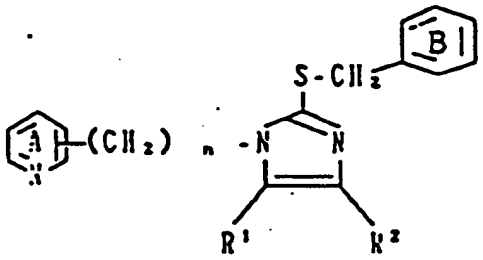
9. Utilisation selon la revendication 6, dans laquelle le dérivé de l'imidazole est le 1-(3-méthyl-2-pyridyle)-2-[2-(diméthylamino)-benzylsulfinyl]imidazole ou un de ses sels d'addition aux acides pharmaceutiquement acceptable.

10. Procédé pour la préparation d'un dérivé de l'imidazole répondant à la formule :



(I)

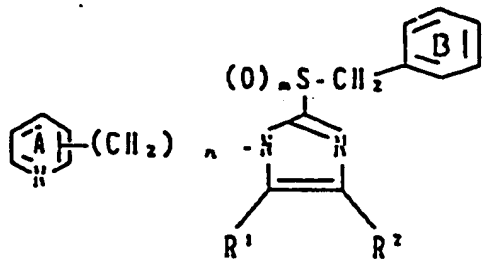
dans laquelle le Cycle A est un groupe 2- ou 4-pyridyle ou un groupe 2- ou 4-pyridyle ayant un substituant choisi parmi un groupe alkyle en C_1 à C_4 et un groupe alcoxy en C_1 à C_4; le Cycle B est un groupe phényle ayant un substituant choisi parmi un groupe amino, un groupe mono(alkyle en C_1 à C_4)amino, un groupe di(alkyle en C_1 à C_4)amino et un groupe morpholino; R^1 et R^2 sont des atomes d'hydrogène ou s'associent pour former un groupe répondant à la formule : $-(CH_2)_q-$: m est 1; n est 0 ou 1; et q est 3 ou 4, ou un de ses sels, qui comprend l'oxydation d'un dérivé de l'imidazole répondant à la formule :



(II)

dans laquelle le Cycle A, le Cycle B, R^1, R^2 et n sont tels que définis ci-dessus, ou un de ses sels, et, si nécessaire, la transformation ultérieure du produit en l'un de ses sels.

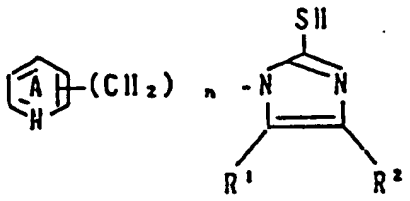
11. Procédé pour la préparation d'un dérivé de l'imidazole répondant à la formule :



(I)

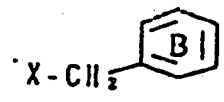
dans laquelle le Cycle A est un groupe 2- ou 4-pyridyle ou un groupe 2- ou 4-pyridyle ayant un substituant choisi parmi un groupe alkyle en C_1 à C_4 et un groupe alcoxy en C_1 à C_4; le Cycle B est un groupe phényle ayant un substituant choisi parmi un groupe amino, un groupe mono(alkyle en C_1 à C_4)amino, un groupe di(alkyle en C_1 à C_4)amino et un groupe morpholino; R^1 et R^2 sont des atomes d'hydrogène ou s'associent pour former un groupe répondant à la formule : $-(CH_2)_q-$; m est 1; n est 0

ou 1; et q est 3 ou 4, ou un de ses sels, qui comprend les stades consistant à :
condenser un mercaptoimidazole répondant à la formule :



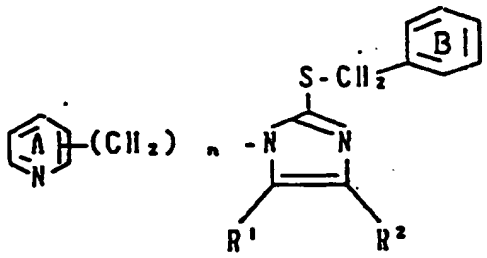
(III)

dans laquelle le Cycle A, R^1, R^2 et n sont tels que définis ci-dessus, ou un de ses sels avec un dérivé du toluène répondant à la formule :



(IV)

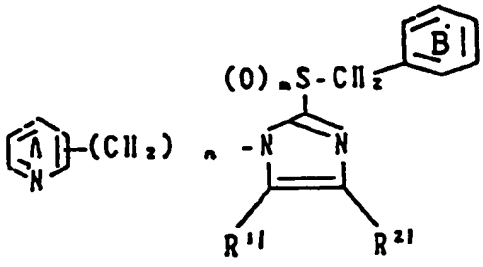
dans laquelle X est un radical réactif et le Cycle B est tel que défini ci-dessus, ou un de ses sels, oxyder le produit obtenu répondant à la formule :



(II)

dans laquelle le Cycle A, le Cycle B, R^1, R^2 et n sont tels que définis ci-dessus, et, si nécessaire, transformer encore le produit en l'un de ses sels.

12. Procédé de préparation d'un dérivé de l'imidazole répondant à la formule :

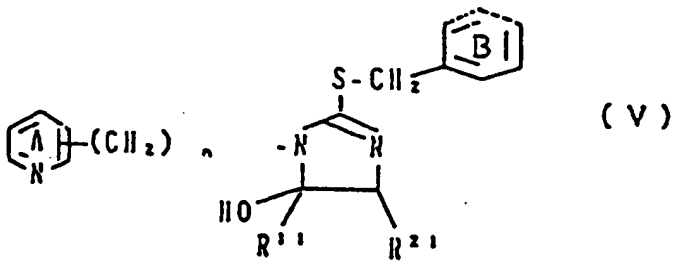


(I)

dans laquelle le Cycle A est un groupe 2- ou 4-pyridyle ou un groupe 2- ou 4-pyridyle ayant un

substituant choisi parmi un groupe alkyle en C_1 à C_4 et un groupe alcoxy en C_1 à C_4; le Cycle B est un groupe phényle ayant un substituant choisi parmi un groupe amino, un groupe mono(alkyle en C_1 à C_4)amino, un groupe di(alkyle en C_1 à C_4)amino et un groupe morpholino; R^{11} et R^{21} s'associent pour former un groupe répondant à la formule: $-(CH_2)_q-$; m est 1; n est 0 ou 1; et q est 3 ou 4, ou un de ses sels, qui comprend les stades consistant à :

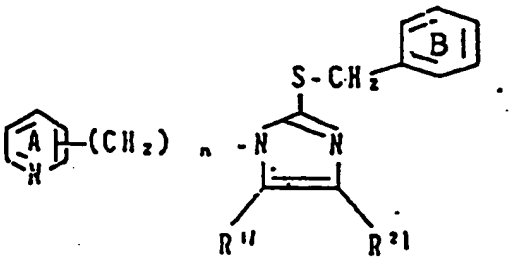
déshydrater un composé répondant à la formule :



(V)

dans laquelle R^{11}, R^{21}, le Cycle A, le Cycle B, et n sont tels que définis ci-dessus,

oxyder le produit obtenu répondant à la formule :



(II')

dans laquelle le Cycle A, le Cycle B, R^{11}, R^{21} et n sont tels que définis ci-dessus, et, si nécessaire, transformer encore le produit en l'un de ses sels.